European Journal of Pediatrics (2021) 180:253–262
https://doi.org/10.1007/s00431-020-03757-7

ORIGINAL ARTICLE

# Predictors for the use of herbal and dietary supplements in children and adolescents with kidney and urinary tract diseases

Tugba Tastemel Ozturk[1] · Nuray Kanbur[2] · Elif Nursel Ozmert[3] · Bora Gulhan[1] · Fatih Ozaltin[1] · Rezan Topaloglu[1] · Ali Duzova[1]

Received: 21 March 2020 / Revised: 21 July 2020 / Accepted: 27 July 2020 / Published online: 6 August 2020


## Abstract

Complementary and alternative medicine are treatments administered alone or in combination with conventional medical treatments. Data on complementary and alternative medicine use in children with kidney and urinary tract diseases are limited. In this cross-sectional study, the frequency and preferred methods of complementary and alternative medicine use and factors associated with their use were evaluated in 201 patients (48% female; median age, 11 years; median disease duration, 5.1 years) with kidney and urinary tract diseases and 260 healthy (without chronic disease) controls. Data were collected through a questionnaire-based interview and patients' medical records. Herbal and dietary supplements, including fish oil, were the most commonly used complementary and alternative medicine agents in both groups. There was no difference in herbal and dietary supplement use between the groups when fish oil was excluded (29% vs. 28%; $p = 0.88$). Herbal and dietary supplements were mainly used to improve/mitigate renal disease (52%). Logistic regression analysis revealed that disease duration > 7 years (odds ratio (OR), 3.70; 95% confidence interval (CI), 1.48–9.20), current use of six or more drugs (OR, 5.6; 95% CI, 1.28–24.41), and recurrent urinary tract infection or nephrolithiasis (OR, 3.92; 95% CI, 1.02–15.09) were the independent risk factors for herbal and dietary supplement use, except fish oil. Middle socioeconomic status was associated with decreased herbal and dietary supplement use, except fish oil, compared with low socioeconomic status (OR, 0.30; 95% CI, 0.11–0.81). Herbal and dietary supplements were used by 78% patients, despite knowing that these products could have side effects; only 42% of the patients shared the information about herbal and dietary supplement use with their doctors.

*Conclusion*: Herbal and dietary supplement use is frequent in children with kidney and urinary tract diseases. Educating health professionals regarding such use is mandatory for developing strategies to prevent critical consequences.

Communicated by Gregorio Paolo Milani

**Electronic supplementary material** The online version of this article (https://doi.org/10.1007/s00431-020-03757-7) contains supplementary material, which is available to authorized users.

✉ Ali Duzova
aduzova@hacettepe.edu.tr

Tugba Tastemel Ozturk
t_tastemel@hotmail.com

Nuray Kanbur
nuraykanbur@hotmail.com

Elif Nursel Ozmert
nozmert@hacettepe.edu.tr

Bora Gulhan
bora.gulhan@hacettepe.edu.tr

Fatih Ozaltin
ozaltinf@gmail.com

Rezan Topaloglu
rezantopaloglu@hacettepe.edu.tr

[1] Division of Pediatric Nephrology, Hacettepe University Faculty of Medicine, Sihhiye, 06100 Ankara, Turkey

[2] Division of Adolescent Medicine, Hacettepe University Faculty of Medicine, Ankara, Turkey

[3] Division of Social & Developmental Pediatrics, Hacettepe University Faculty of Medicine, Ankara, Turkey

**What is Known:**
• *Complementary and alternative medicine (CAM) practices are therapeutic approaches that do not have sufficient efficacy and safety evidence.*
• *CAM is widely used in healthy children and in certain chronic diseases.*

**What is New:**
• *Herbal and dietary supplements (HDSs) were the most commonly used method in kidney and urinary tract diseases.*
• *Duration of disease, number of drugs, and socioeconomic status are determinants of HDS use except fish oil.*

**Keywords** Childhood · Complementary and alternative medicine · Herbal and dietary supplement · Kidney · Urinary tract

**Abbreviations**

| | |
|---|---|
| CAM | Complementary and alternative medicine |
| CKD | Chronic kidney disease |
| HDS | Herbal and dietary supplements |
| NCCAM | National Center for Complementary and Alternative Medicine |
| UTI | Urinary tract infection |

## Introduction

Insufficient evidence is available regarding the safety and efficacy of complementary and alternative medicine (CAM) practices; therefore, these therapeutic approaches are not included in conventional medical therapy [1, 2]. A systematic review of 58 studies on children without chronic diseases revealed that the lifetime CAM use rate was 11–88% and that the CAM use incidence in the USA in the last 12 months was 12% [1, 3]. Lifetime prevalence of CAM use in healthy children was 56% and 83% in two studies from Turkey [4, 5]. The CAM approaches are used for children with chronic diseases. In Germany, the incidence of CAM use in healthy children and children with chronic diseases (cardiac, neurologic, respiratory/skin, and miscellaneous chronic disease) was 53% (86/163) and 59% (143/242), respectively [6]. The frequency of CAM use in adults with chronic kidney disease (CKD) was 52–64% across Turkey, Palestine, Egypt, and the USA [7–10]. To the best of our knowledge, data on CAM use for children with kidney and urinary tract diseases are not available.

According to the National Center for Complementary and Alternative Medicine (NCCAM), the main categories of CAM are biologically based practices, manipulative and body-based methods, mind-body medicine, energy therapies, and whole medical systems [11]. In many studies involving healthy children and children with chronic illnesses, the most commonly used CAM method was administration of herbal and dietary supplements (HDSs; biologically based practices) [2, 4, 12–14]. HDSs are often used with medications, especially in children with chronic diseases, and several products are used simultaneously [4]. Side effects can be secondary to drug-product or product-product interaction and may develop because of the product itself or contaminated product. The use of these products may lead to severe organ failure/loss or death [15]. Moreover, patients/parents do not usually inform health professionals about CAM use [4, 6, 16, 17].

In this cross-sectional study, we aimed to describe the frequency of CAM use in pediatric patients with renal and urinary tract diseases, to define the preferred methods and factors that affect their use, and to compare these findings with those for healthy children.

## Materials and methods

### Study design and population

This study was conducted at the Division of Pediatric Nephrology, İhsan Doğramacı Children's Hospital, Hacettepe University. All patients aged < 20 years diagnosed with recurrent urinary tract infections (UTIs), nephrolithiasis, or nephrotic syndrome and patients who had undergone renal replacement therapy (peritoneal dialysis, hemodialysis, and renal transplantation) with a follow-up period ≥ 3 months were enrolled; only the parents of two children refused to participate. Age- and sex-matched children without chronic diseases who consulted the General Pediatrics, Adolescent, and Social Pediatrics Outpatient Clinics constituted the control group. The study protocol was approved by the Non-Interventional Clinical Researches Ethics Board of Hacettepe University.

### Variables and measurements

Demographic information was obtained from family members and medical records (type of disease, age at diagnosis, previous and current medication history, hospital stay (inpatient) history, level of adherence to medication, comorbidities, and renal disease in the family). Level of adherence to medication was assessed using the Morisky adherence scale, and three levels of adherence were defined according to the summed scores, namely high adherence (0), medium adherence (1–2), and low adherence (3–4) [18].

CAM use by patients and healthy children was investigated through a questionnaire-based interview conducted by the same investigator (TTO) with patients/healthy children and their parents. Families were informed of the definition and methodology of CAM practices, in accordance with the categories of the NCCAM. The questionnaire inquired after CAM usage, CAM methods, reasons for using CAM, sources of information of CAM practices and products, side effects observed, sharing of CAM usage history with health professionals, opinions on potential side effects of HDSs, inquiry about CAM use by physicians during previous hospital visits, age and health status of parents, number and health status of siblings, residence, perceived socioeconomic status (self-categorization as low, middle, or high) [19], and social security conditions. Questionnaire clarity was tested in a pilot study with 10 patients and their parents. The observation period for CAM use covered the disease duration for the patients and the entire life for the controls.

The relationship between CAM use and anxiety levels of patients, healthy children, and parents was also assessed. After the questionnaire was administered, the Continuous Anxiety subscale of the State-Trait Anxiety Inventory, developed by Spielberger and adapted by Öner and Le Compte for the Turkish population, was applied to all parents, healthy children, and patients aged ≥ 14 years and the Continuous Anxiety subscale of the State-Trait Anxiety Inventory for Children, developed by Spielberger and adapted by Ozusta for the Turkish population, was applied to patients and healthy children aged 9–14 years [20, 21]. Internal consistency of the responses to the anxiety scales was assessed by calculating the Cronbach alpha coefficient. The coefficients for the scales applied to children aged 9–14 and ≥ 14 years were 0.84 and 0.84, respectively; the coefficient for the scales applied to the parents was 0.79.

### Statistical analysis

Statistical Package for Social Sciences for Windows 22′ program was used for analysis. Variables with normal distribution in descriptive statistics were presented as mean ± standard deviation; those without normal distribution, median (25th–75th percentiles); and categorical variables, number of cases and percentage (%). Student's $t$ test was used to compare numerical variables with normal distribution; the Mann-Whitney $U$ test was used to compare numerical variables without normal distribution. Categorical variables were assessed using Pearson's chi-square or Fisher's exact test. Using the possible factors identified in univariate analyses ($p \leq 0.20$), the independent predictors for the use of HDSs, except fish oil, were examined in multivariate analysis using logistic regression analysis. $p$ value $\leq 0.05$ was considered statistically significant.

## Results

### Study population

We enrolled 201 patients (104 boys; 97 girls) and 260 healthy children (128 boys; 132 girls). There were no missing data for medical records or questionnaire-based interview. Median age of the patient group and control group was 11 years (25th–75th percentiles: 6.4–14.9) and 9.7 years (25th–75th percentiles: 6.9–14.0; $p = 0.159$), respectively. The clinical characteristics of the patients are presented in Table 1. The sociodemographic characteristics and anxiety scores of the patient and control groups are shown in Table 2.

### Prevalence of CAM users

In the patient group, the frequency of CAM use was 41% (83/201) after kidney or urinary tract disease diagnosis; it was 55% in the control group. Compared with that for the control group, the odds ratio (OR) for CAM use, adjusted for the observation period, was 0.43 (95% confidence interval (CI),

**Table 1** Clinical characteristics of the patients ($n = 201$)

| Clinical characteristics | Results |
|---|---|
| Disease groups | |
| Recurrent urinary tract infections | 52 (26%) |
| Nephrotic syndrome | 46 (23%) |
| Nephrolithiasis | 23 (11%) |
| Chronic kidney disease (stages II–IV) | 31 (15%) |
| Renal replacement therapy | 49 (24%) |
| Kidney transplantation | 23 (11%) |
| Peritoneal dialysis | 16 (8.0%) |
| Hemodialysis | 10 (5.0%) |
| Age at diagnosis, years | 3.3 (0.8–7.0) |
| Duration of disease, years | 5.1 (2.3–9.5) |
| Presence of hospital stay (inpatient) | 148 (74%) |
| Total number of hospital stay (inpatient) episodes | 4 (2–7.75) |
| Total hospital stay (inpatient) days | 34.5 (9–94.5) |
| Current drug use | 158 (79%) |
| Number of drugs currently used | 5 (2–8) |
| Adherence to medication* | |
| High | 47 (30%) |
| Medium | 104 (66%) |
| Low | 7 (4.4%) |
| Presence of additional health problems | 90 (45%) |
| Presence of renal disease in the family | 64 (32%) |

Frequencies are shown as $n$ (%); other values are presented as median (25th and 75th percentiles)

*Morisky adherence scale was used; high adherence (score: 0), medium adherence (score: 1–2), low adherence (score: 3–4)

**Table 2** Sociodemographic characteristics and anxiety scores of the patient and control groups

| Variable | Patient group ($n = 201$) | Control group ($n = 260$) | $p$ value |
|---|---|---|---|
| Survey respondent, *n* (%) | | | |
| Mother | 141 (70) | 223 (86) | < 0.001*,c |
| Father | 57 (28) | 34 (13) | |
| Other | 3 (1.5) | 3 (1.2) | |
| Gender, *n* (%) | | | |
| Male | 104 (52) | 128 (49) | 0.593 c |
| Female | 97 (48) | 132 (51) | |
| Residency, *n* (%) | | | |
| City | 134 (67) | 204 (78) | < 0.001*,c |
| Town | 51 (25) | 53 (20) | |
| Rural area | 16 (8.0) | 3 (1.2) | |
| Maternal education level, *n* (%) | | | |
| Primary school or uneducated[a] | 95 (47) | 82 (32) | < 0.001*,c |
| Secondary school | 38 (19) | 34 (13) | |
| High school | 43 (21) | 77 (30) | |
| University | 25 (12) | 67 (26) | |
| Paternal education level, *n* (%) | | | |
| Primary school or uneducated[b] | 60 (30) | 51 (20) | 0.033*,c |
| Secondary school | 33 (16) | 36 (14) | |
| High school | 61 (30) | 92 (35) | |
| University | 47 (23) | 81 (31) | |
| Socioeconomic status level, *n* (%) | | | |
| High | 50 (25) | 40 (15) | 0.03*,c |
| Middle | 126 (63) | 177 (68) | |
| Low | 25 (12) | 43 (17) | |
| Health insurance, *n* (%) | | | |
| Yes | 197 (98) | 257 (99) | 0.476[d] |
| No | 4 (2.0) | 3 (1.2) | |
| Presence of chronic illness at home, *n* (%) | 120 (60) | 149 (57) | 0.605[c] |
| The presence of family elders living in the home, *n* (%) | 23 (11) | 31 (12) | 0.874[c] |
| Number of people living at home | | | |
| 2–4 | 119 (59) | 182 (70) | 0.016*,c |
| ≥ 5 | 82 (41) | 78 (30) | |
| Parental anxiety score** | 49 (45–53) | 48 (44–53) | 0.358[e] |
| Anxiety score for 9–14-year-old children*** | 34 ± 7 | 36 ± 7 | 0.017*,f |
| Anxiety score for 14–18-year-old children** | 46 (44–50) | 46 (43–51) | 0.934[e] |

*Statistically significant values ($p < 0.05$)

**Data are presented as median (25th and 75th percentiles)

***Data are presented as mean ± standard deviation

[a] In the patient group, the number of illiterate mothers was 7; literate mothers, 4; and mothers who had graduated primary school, 84. In the control group, the number of illiterate mothers was 2; literate mothers, 4; and mothers who had graduated primary school, 76. Illiterate, literate, and primary school graduate education groups were combined for statistical analysis

[b] In the patient group, the number of literate fathers was 4 and that of fathers who had graduated primary school was 56. There were no literate fathers in the control group, and the number of fathers who had graduated primary school was 51. Literate and primary school graduate education groups were combined for statistical analysis

[c] Pearson's chi-square test

[d] Fisher's exact test

[e] Mann-Whitney *U* test

[f] Student's *t* test

**Table 3** Frequency of complementary and alternative medicine methods in the patient and control groups

| Methods | Patient group ($n = 201$) | Control group ($n = 260$) | $p$ value |
|---|---|---|---|
| Any CAM method | 83 (41) | 142 (55) | 0.005* |
| Biologically based therapies (HDSs) | 78 (39) | 142 (55) | 0.001* |
| Fish oil | 29 (14) | 91 (35) | < 0.001* |
| HDSs except fish oil | 58 (29) | 73 (28) | 0.877 |
| Mind-body interventions | 8 (3.9) | 2 (0.7) | 0.042* |
| Blessing by hodja | 3 (1.5) | 2 (0.7) | 0.447 |
| Amulet | 3 (1.5) | 0 | 0.994 |
| Tomb visit | 2 (0.9) | 0 | 0.995 |
| Whole medical systems | 3 (1.5) | 2 (0.7) | 0.512 |
| Acupuncture | 2 (0.9) | 0 | 0.990 |
| Leech therapy | 1 (0.5) | 1 (0.35) | 0.825 |
| Ayurvedic medicine | 0 | 1 (0.35) | 0.994 |
| Manipulative and body-based methods (massage therapy) | 1 (0.5) | 0 | 0.986 |
| Energy therapies | 0 | 0 | |

*CAM* complementary and alternative medicine, *HDSs* herbal and dietary supplements

Results are presented as $n$ (%); $p$ values are adjusted for the duration of the observation period and are calculated using logistic regression

*Statistically significant values ($p < 0.05$)

The total number is higher owing to the use of more than one practice in some individuals

0.16–0.61) in the patient group ($p = 0.005$). The most commonly used CAM strategy was biologically based therapies in both groups, while other methods were rarely used. Table 3 shows the frequency of use of CAM methods in both groups.

Fish oil use was the most prevalent CAM method in both groups (29/201 (14%) in the patient group, and 91/260 (35%) in the control group; OR adjusted for observation period, 0.70; 95% CI, 0.51–0.81; $p < 0.001$)). As fish oil use is widespread in the community, the frequency and characteristics of HDSs were re-analyzed after excluding fish oil use. Fifty-eight (29%) children in the patient group and 73 (28%) children in the control group used HDSs, except fish oil, and the frequency of HDS use was comparable ($p = 0.877$).

The frequency of use of HDSs or of HDSs, except fish oil, did not differ significantly among the disease groups ($p = 0.498$ and $p = 0.209$, respectively). Only three of the 23 (13%) transplanted patients had used HDSs after transplantation.

The types of HDSs used varied widely, with the most commonly used products being fish oil, kefir, and vitamins (Online Resource 1). Gilaburu (*Viburnum opulus*) was used by patients with nephrolithiasis, while children with recurrent UTIs used blueberries, parsley juice, cauliflower juice, oleaster juice, and water with vinegar.

## Reasons for HDS use and HDS information sources

Most patients used HDSs, except fish oil, to improve/mitigate kidney disease (52%) and upper respiratory tract infection (17%) and to improve immunity (14%; Fig. 1). HDSs, except fish oil, were rarely used in cases of oral aphthae ($n = 1$), diabetes mellitus ($n = 1$), and constipation ($n = 2$) and in the prevention of vascular occlusion ($n = 1$). Most families in both groups had learned of the products from friends, relatives, or neighbors. Doctors, the media, and places where the products were sold were other sources of information in both groups (Fig. 2).

## Correlates of HDS use

In patients, disease duration > 7 years (OR, 3.70; 95% CI, 1.48–9.20; $p = 0.005$), current use of six or more drugs (OR, 5.60; 95% CI, 1.28–24.41; $p = 0.022$), and recurrent UTIs or nephrolithiasis (OR, 3.92; 95% CI, 1.02–15.09; $p = 0.047$) were the independent risk factors for HDS use, except fish oil use (Table 4). Middle socioeconomic status was associated with decreased use of HDSs, except fish oil, in patients compared with low socioeconomic status (OR, 0.30; 95% CI, 0.11–0.81; $p = 0.017$). In the control group, higher maternal education level (OR, 4.13; 95% CI, 1.63–10.43; $p = 0.003$) and use of HDSs by other family members (OR, 3.71; 95% CI, 2.01–6.85; $p < 0.001$) were the independent factors associated with high use of HDSs, except fish oil. Adherence to medication and anxiety scores had no significant effect on the use of HDSs, except fish oil use.

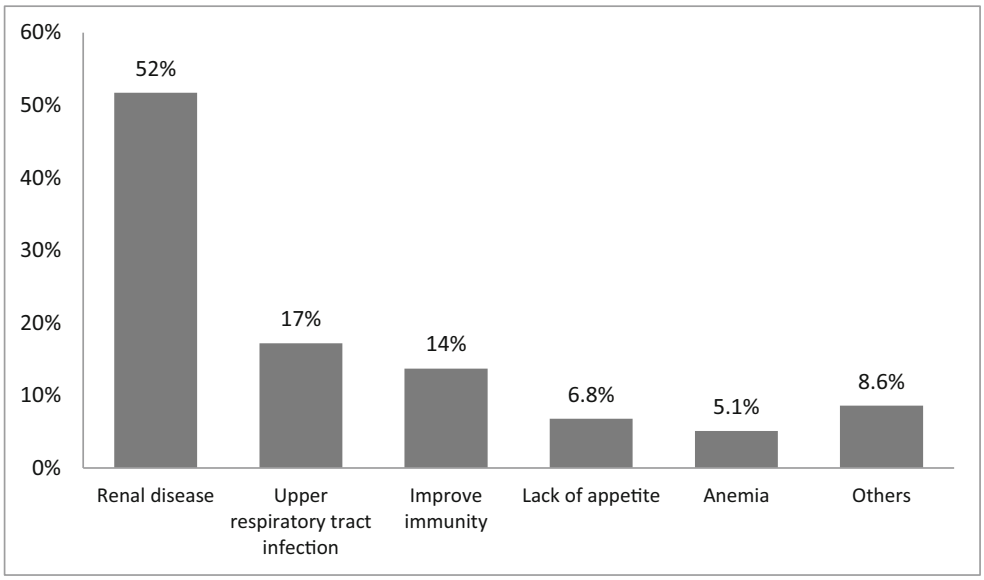


**Fig. 1** Patients' reasons for the use of herbal and dietary supplements (fish oil excluded; $n = 58$)

## HDS users' thoughts on these products, informing their doctors of HDS use, and side effects

Of the parents who used HDSs, 61 (61/78, 78%) in the patient group and 107 (107/142, 75%) in the control group used these products, although they thought that these products may cause side effects ($p = 0.340$); 60 (60/78, 77%) parents in the patient group and 115 (115/142, 81%) in the control group thought that these products could interact with other drugs ($p = 0.705$). However, only 33 (33/78, 42%) HDS users in the patient group and 65 (65/142, 46%) in the control group informed their physicians about HDS use ($p = 0.971$). Frequency of inquiry about CAM use by the physicians during a visit was also very low in both groups (patient group: 17/201, 8.5%; control group: 33/260, 13%; $p = 0.147$).

Based on the patients' reports, five (6.4%) of the 78 patients had experienced adverse effects following HDS use. Kidney function was impaired in two patients; while the name of the product used by one of these patients was unknown, the other had developed biopsy-proven tubulointerstitial nephritis after St. John's wort use. Patients reported that they had experienced diarrhea, itching, and nausea following the use of cauliflower juice for recurrent UTIs, herbal tea for kidney disease, and fish oil for hyperlipidemia, respectively. In the control group, eight (5.6%) of the 142 children using HDSs reported side effects; all side effects were associated with fish oil use (nausea ($n = 5$), loss of appetite ($n = 1$), redness in the skin ($n = 1$), and weight gain ($n = 1$)).

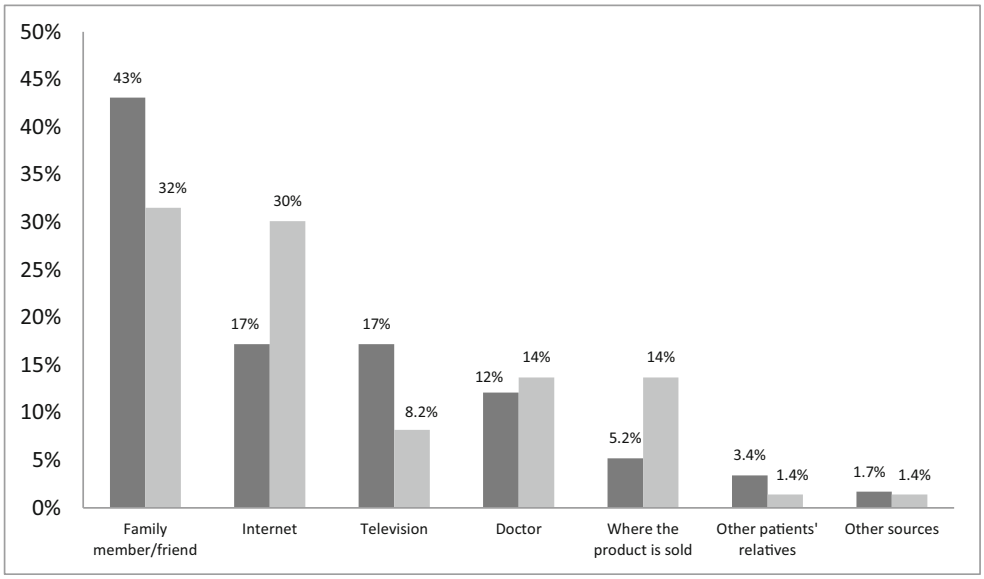


**Fig. 2** Information sources regarding the use of herbal and dietary supplements (fish oil excluded) in the patient ($n = 58$) and control ($n = 73$) groups

**Table 4** Results of logistic regression analysis for the factors associated with the use of herbal and dietary supplements (fish oil excluded)

| Risk factors | OR (95% CI) | *p* value |
|---|---|---|
| Patient group | | |
| Duration of disease | | |
| 3 months–3 years (reference) | | |
| 3–7 years | 1.59 (0.63–3.99) | 0.316 |
| > 7 years | 3.70 (1.48–9.20) | 0.005* |
| Number of drugs currently used | | |
| 0–1 (reference) | | |
| 2–5 | 3.89 (1.28–11.79) | 0.016* |
| ≥ 6 | 5.60 (1.28–24.41) | 0.022* |
| Disease type | | |
| CKD (reference) | | |
| Nephrotic syndrome | 2.08 (0.70–6.14) | 0.184 |
| UTI or nephrolithiasis | 3.92 (1.02–15.09) | 0.047* |
| Total number of hospital stays (inpatient) | | |
| 0–3 times (reference) | | |
| > 4 times | 2.02 (0.87–4.71) | 0.100 |
| Socioeconomic status | | |
| Low (reference) | | |
| Middle | 0.30 (0.11–0.81) | 0.017* |
| High | 0.60 (0.20–1.78) | 0.359 |
| Control group | | |
| Maternal education level | | |
| Primary school or not educated (reference) | | |
| Secondary school | 2.83 (0.99–8.04) | 0.052 |
| High school | 3.60 (1.48–9.70) | 0.005* |
| University | 4.13 (1.63–10.43) | 0.003* |
| Number of people living at home | | |
| 2–4 (reference) | | |
| ≥ 5 | 0.51 (0.23–1.10) | 0.086 |
| Use of HDSs by other members of the family | | |
| No (reference) | | |
| Yes | 3.71 (2.01–6.85) | < 0.001* |

*CKD* chronic kidney disease, *HDSs* herbal and dietary supplements, *UTI* urinary tract infection

*Statistically significant values ($p < 0.05$)

The dependent variable was use of herbal and dietary supplements (fish oil excluded). The possible factors identified in univariate analyses ($p \leq 0.20$) were examined as independent predictors for the use of HDSs, except fish oil, by logistic regression analysis

The independent variables for the patient group were age, duration of the disease, number of drugs currently used, disease type, total number of hospital stay (inpatient) episodes, socioeconomic status, use of HDSs by other members of the family, and family elders living at home

The independent variables for the control group were maternal education level, paternal education level, number of people living at home, family elders living at home, use of HDSs by other members of the family, and socioeconomic status

## Discussion

Frequency of CAM usage in the patient and control groups was 41% and 55%, respectively. Though fish oil use was more common in the control group, frequency of HDS use in both groups was comparable when fish oil was excluded. Among 135 children over 1 year of age with various chronic diseases (including kidney diseases) from Bursa, Turkey, prevalence of CAM use (42%) was similar to that found in our study [22]. In adults with CKD, the frequency of CAM use was variable (12–64%) [7, 9, 17, 23, 24].

In the UK, children with chronic diseases (cerebral palsy, inflammatory bowel disease, and cancer) were more likely to use CAM methods compared with healthy children (40% vs. 12%; $p = 0.009$) [25]. In a similar study from Germany, the frequency of CAM use in children with chronic diseases (cardiac diseases, neurological diseases, respiratory system and skin diseases, and various other diseases) and in healthy children was comparable (60% and 53%, respectively) [6]. These differences in frequency may be due to different definitions of CAM in the studies, sociocultural differences, size of the study populations, and the chronic diseases included.

In our study, the most frequent CAM approach in both groups was HDS use. The same pattern was observed in many studies involving children with chronic diseases and healthy children [2, 4, 12–14, 26–31]. However, Ayurvedic medicine (India), mind-body medicine (the USA), and homeopathy (Switzerland) were the leading methods in other studies [9, 23, 24]. Besides, in the above-mentioned study from Turkey, the most common CAM approaches were special diets and massages [22]. Common approaches may be different in different geographical areas or cultures, even within the same country.

A national survey conducted in the USA in 2012 revealed that fish oil was the most commonly used biologically based product over a 30-day period [3]. In Ireland, the frequency of lifetime fish oil use in children admitted to the hospital was 15% [32]. We showed that fish oil was the most commonly used HDS in both groups; however, frequency of fish oil use was higher in the control group (35% vs. 14%, $p < 0.001$). We can speculate that since most children in the patient group (158/201; 79%) were taking medication, some of them might not be willing to take fish oil (an additional product). It is also possible that their parents might think that fish oil is not helpful in the situation, or they might have concerns about fish oil and prescribed medication interactions.

We observed that fish oil, kefir, and vitamins were the most frequently used HDSs in the patient group. These products are similar to commonly used products in the control group. The most commonly used HDSs for kidney diseases were parsley juice, black seed oil, gilaburu (*Viburnum opulus*), and blueberries. In two studies among adults with CKD from Palestine and Egypt, the most commonly used herbal product was black cumin (19%), followed by sage (17%), anise (11%), and chamomile (11%) [7, 8]. Differences in the types of products used may be due to geographical features, sociocultural

differences, marketing strategies in a particular country, and patient characteristics.

In our cohort, the most common reason for HDSs except fish oil use in the patient group was kidney disease improvement/mitigation. A study in adult patients with CKD or kidney transplantation showed that improvement of renal function was the most common reason for HDS use, whereas in hemodialysis patients, the most common reasons were mood improvement and mitigating the side effects of conventional medical treatments [8, 17]. These results suggest that CKD patients are not satisfied with conventional medical treatment modalities and are in search of different and complementary treatments.

In many studies among adults with CKD, children with other chronic diseases, and healthy children, relatives, and friends were seen as the most prevalent sources of information about CAM [4–6, 8, 12, 13, 16, 17, 34, 35]. Our results support these previous studies.

We showed that low socioeconomic status, longer disease duration, higher number of drugs currently being used, and type of disease were independent factors associated with the use of these products. Although 98% of the families had health insurance, parents with low socioeconomic status may have experienced difficulties in reaching health facilities, such as travel expenses and participation fees. Among adult patients on hemodialysis, no correlation was reported between the duration of dialysis and the use of CAM [9]. In contrast, adult patients on dialysis for 1–4 years used CAM more frequently than those with shorter dialysis durations [23]. In a study among adults with CKD and another study on epileptic children, no relationship was found between the number of drugs currently being used and CAM use [7, 14].

In a review of 18 studies analyzing the relationship between parental education and CAM use in healthy children, CAM methods were used more frequently in children with higher levels of parental education in 10 studies, while no such relationship was noted in the other 8 [1]. We showed that, in the control group, mothers who graduated from university used HDSs except fish oil four times more frequently than uneducated or primary school graduate mothers. This may be because people with a high level of education could access information about these products more easily.

The aforementioned systematic review also reported that parental CAM use was the strongest indicator for CAM use in children [1]. Similarly, in our study, the use of HDSs by other family members increased the use of these products for the children.

In a study including 135 mothers of children with chronic diseases, a positive relationship was found between the high anxiety levels of the mothers and herbal product use in the children [22]. In contrast, no relationship was found between depression and anxiety levels of children and frequency of CAM use in pediatric patients in a tertiary pain center [36]. Our study showed no relationship between anxiety levels of children or their parents and frequency of HDS use in the patient and control groups.

In this study, almost 75% of the individuals who used these products in both groups were aware of their potential side effects, and most parents thought that these products could interact with other drugs. Besides, the incidence of sharing the use of these products with their doctors in both groups was very low (42% in the patient group and 46% in the control group). Two studies in adults with CKD showed that 37–67% of patients did not share CAM use information with their physicians [16, 17]. We also found that physicians have rarely enquired about the use of these products: in Australia, 50% of the parents of healthy children who did not share the information about CAM use with their physicians stated that they did not do so because the physicians did not ask [12].

In Thailand, adverse effects were seen in 8 of the 166 adult patients with CKD (4.8%) who were using these products; serum creatinine levels increased in three patients [33]. In a systematic review of case reports presenting side effects related to the use of herbal products in children, it was determined that three children needed organ transplants and nine had lost their lives due to the side effects [15]. In our study, two patients (2/78, 2.5%) had renal impairment following HDS use. However, the actual figure is probably much higher, since this reported figure is solely based on patients' reports and not on regular follow-up and monitoring of renal function. We are also aware that some products may be benign and safe, although they may be ineffective. Education of professionals and prompt communication between physicians and patients/parents are critical for the prevention of these side effects.

Our study has several limitations. First, questionnaire-based research has certain disadvantages, such as inappropriate interpretation of the questions, a lapse of memory, and the answers not reflecting the actual attitudes of respondents. We tried to minimize these limitations by having the interviews conducted by the same investigator, enrollment of volunteers, and also providing adequate time to answer the questions. Second, we had to include different types of kidney disease, from UTIs to conditions requiring renal replacement therapy, and studies in specific sub-groups with larger participants may provide further information. Third, the control group comprised patients recruited in the hospital instead of healthy children. Moreover, different definitions of CAM in the studies, even in the same country, make comparison between geographical areas, cultures, and disease groups difficult. Given these limitations, we invite the readers to be careful when interpreting the results.

## Conclusion

The frequency of HDSs except fish oil use in children with kidney and urinary tract diseases was comparable with that of the control group. Patients with longer disease duration, high number of drugs currently used, nephrolithiasis, or recurrent UTIs, and patients with low socioeconomic status are under a higher risk of HDS use. Geographical, social-cultural, and economic conditions may affect CAM use. We recommend the education of health professionals on this topic in order to develop approaches that encourage patients/parents to share their search, practice, and concerns regarding CAM, so as to prevent critical consequences.

**Acknowledgments** The manuscript was reviewed for English language by a native English speaker from the Hacettepe University Technology Transfer Center, and has been edited by professional editors at Editage, a division of Cactus Communications (Job Code: HTTTM_582_2).

**Authors' Contributions** All authors contributed to the study conception and design. Material preparation and analysis were performed by TTO and AD. Questionnaires were administered by TTO. The first draft of the manuscript was written by TTO and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

**Data availability** Not applicable

## Compliance with ethical standards

**Conflict of interest** The authors declare that they have no conflicts of interest.

**Ethics approval** Approval was obtained from the Non-Interventional Clinical Researches Ethics Board of Hacettepe University. The procedures used in this study adhere to the tenets of the Declaration of Helsinki.

This article does not contain any procedures with human participants or animals performed by any of the authors.

**Informed consent** Informed consent was obtained from all individual participants included in the study.

**Consent to publish** Not applicable

**Code availability** Not applicable

## References

1. Italia S, Wolfenstetter SB, Teuner CM (2014) Patterns of complementary and alternative medicine (CAM) use in children: a systematic review. Eur J Pediatr 173:1413–1428. https://doi.org/10.1007/s00431-014-2300-z
2. Barnes PM, Bloom B, Nahin RL (2008) Complementary and alternative medicine use among adults and children: United States, 2007. Natl Health Stat Rep 12:1–23
3. Black LI, Clarke TC, Barnes PM, Stussman BJ, Nahin RL (2015) Use of complementary health approaches among children aged 4-17 years in the United States: National Health Interview Survey, 2007-2012. Natl Health Stat Report 78:1–19
4. Ozturk C, Karayagiz G (2008) Exploration of the use of complementary and alternative medicine among Turkish children. J Clin Nurs 17:2558–2564. https://doi.org/10.1111/j.1365-2702.2008.02329.x
5. Tuncel T, Sen V, Kelekci S, Karabel M, Sahin C, Uluca U, Karabel D, Haspolat YK (2014) Use of complementary and alternative medicine in children who have no chronic disease. Turk Pediatri Ars 49:148–153. https://doi.org/10.5152/tpa.2014.1498
6. Gottschling S, Gronwald B, Schmitt S, Schmitt C, Längler A, Leidig E, Meyer S, Baan A, Shamdeen MG, Berrang J, Graf N (2013) Use of complementary and alternative medicine in healthy children and children with chronic medical conditions in Germany. Complement Ther Med 21(Suppl 1):S61–S69. https://doi.org/10.1016/j.ctim.2011.06.001
7. Zyoud SH, Al-Jabi SW, Sweileh WM, Tabeeb GH, Ayaseh NA, Sawafta MN, Khdeir RL, Mezyed DO, Daraghmeh DN, Awang R (2016) Use of complementary and alternative medicines in haemodialysis patients: a cross-sectional study from Palestine. BMC Complement Altern Med 16:204. https://doi.org/10.1186/s12906-016-1196-8
8. Osman NA, Hassanein SM, Leil MM, NasrAllah MM (2015) Complementary and alternative medicine use among patients with chronic kidney disease and kidney transplant recipients. J Ren Nutr 25:466–471. https://doi.org/10.1053/j.jrn.2015.04.009
9. Birdee GS, Phillips RS, Brown RS (2013) Use of complementary and alternative medicine among patients with end-stage renal disease. Evid Based Complement Alternat Med 2013:654109–654106. https://doi.org/10.1155/2013/654109
10. Ceyhan O, Goris S, Dogan N, Korkut Bayindir S (2017) The use of complementary and alternative medicine by patients undergoing hemodialysis. Altern Ther Health Med 23:40–45
11. Fan KW (2005) National Center for Complementary and Alternative Medicine website. J Med Libr Assoc 93:410–412
12. Frawley JE, Anheyer D, Davidson S, Jackson D (2017) Prevalence and characteristics of complementary and alternative medicine use by Australian children. J Paediatr Child Health 53:782–787. https://doi.org/10.1111/jpc.13555
13. Orhan F, Sekerel BE, Kocabas CN, Sackesen C, Adalioglu G, Tuncer A (2003) Complementary and alternative medicine in children with asthma. Ann Allergy Asthma Immunol 90:611–615. https://doi.org/10.1016/S1081-1206(10)61864-9
14. Hartmann N, Neininger MP, Bernhard MK, Syrbe S, Nickel P, Merkenschlager A, Kiess W, Bertsche T, Bertsche A (2016) Use of complementary and alternative medicine (CAM) by parents in their children and adolescents with epilepsy - Prevelance, predictors and parents' assessment. Eur J Paediatr Neurol 20:11–19. https://doi.org/10.1016/j.ejpn.2015.11.003
15. Gardiner P, Adams D, Filippelli AC, Nasser H, Saper R, White L, Vohra S (2013) A systematic review of the reporting of adverse events associated with medical herb use among children. Glob Adv Health Med 2:46–55. https://doi.org/10.7453/gahmj.2012.071
16. Akyol AD, Yildirim Y, Toker E, Yavuz B (2011) The use of complementary and alternative medicine among chronic renal failure patients. J Clin Nurs 20:1035–1043. https://doi.org/10.1111/j.1365-2702.2010.03498.x
17. Bahall M (2017) Use of complementary and alternative medicine by patients with end-stage renal disease on haemodialysis in Trinidad: a descriptive study. BMC Complement Altern Med 17:250. https://doi.org/10.1186/s12906-017-1755-7
18. Morisky DE, Green LW, Levine DM (1986) Concurrent and predictive validity of a self-reported measure of medication adherence. Med Care 24:67–74. https://doi.org/10.1097/00005650-198601000-00007

19. Adler NE, Epel ES, Castellazzo G, Ickovics JR (2000) Relationship of subjective and objective social status with psychological and physiological functioning: preliminary data in healthy white women. Health Psychol 19:586–592. https://doi.org/10.1037/0278-6133.19.6.586
20. Öner N, Le Compte A (1983) Durumluk-sürekli kaygı envanteri el kitabı. Boğaziçi Üniversitesi Yayınları, İstanbul
21. Ozusta S (1995) Çocuklar için durumluk-sürekli kaygı envanteri uyarlama, geçerlik ve güvenirlik çalışması. Türk Psikoloji Dergisi 10:32–44
22. Ozyazicioglu N, Ogur P, Tanriverdi G, Vural P (2012) Use of complementary and alternative medicine and the anxiety levels of mothers of children with chronic diseases. Jpn J Nurs Sci 9:19–27. https://doi.org/10.1111/j.1742-7924.2011.00179.x
23. Arjuna Rao AS, Phaneendra D, Pavani CD, Soundararajan P, Rani NV, Thennarasu P, Kannan G (2016) Usage of complementary and alternative medicine among patients with chronic kidney disease on maintenance hemodialysis. J Pharm Bioallied Sci 8:52–57. https://doi.org/10.4103/0975-7406.171692
24. Hess S, De Geest S, Halter K, Dickenmann M, Denhaerynck K (2009) Prevalence and correlates of selected alternative and complementary medicine in adult renal transplant patients. Clin Transpl 23:56–62. https://doi.org/10.1111/j.1399-0012.2008.00901.x
25. McCann LJ, Newell SJ (2006) Survey of paediatric complementary and alternative medicine use in health and chronic illness. Arch Dis Child 91:173–174. https://doi.org/10.1136/adc.2004.052514
26. Araz N, Bulbul S (2011) Use of complementary and alternative medicine in a pediatric population in southern Turkey. Clin Invest Med 34:E21–E29. https://doi.org/10.25011/cim.v34i1.14909
27. Doering JH, Reuner G, Kadish NE, Pietz J, Schubert-Bast S (2013) Pattern and predictors of complementary and alternative medicine (CAM) use among pediatric patients with epilepsy. Epilepsy Behav 29:41–46. https://doi.org/10.1016/j.yebeh.2013.06.025
28. Haliloglu B, Isguven P, Yildiz M, Arslanoglu I, Erguven M (2011) Complementary and alternative medicine in children with type 1 diabetes mellitus. J Clin Res Pediatr Endocrinol 3:139–143. https://doi.org/10.4274/jcrpe.v3i3.27
29. Dalla Libera D, Colombo B, Pavan G, Comi G (2014) Complementary and alternative medicine (CAM) use in an Italian cohort of pediatric headache patients: the tip of the iceberg. Neurol Sci 35(Suppl 1):145–148. https://doi.org/10.1007/s10072-014-1756-y
30. Karali Y, Demirkaya M, Sevinir B (2012) Use of complementary and alternative medicine in children with cancer: effect on survival. Pediatr Hematol Oncol 29:335–344. https://doi.org/10.3109/08880018.2012.670368
31. Schütze T, Längler A, Zuzak TJ, Schmidt P, Zernikow B (2016) Use of complementary and alternative medicine by pediatric oncology patients during palliative care. Support Care Cancer 24:2869–2875. https://doi.org/10.1007/s00520-016-3097-2
32. Low E, Murray DM, O'Mahony O, O'B Hourihane J (2008) Complementary and alternative medicine use in Irish paediatric patients. Ir J Med Sci 177:147–150. https://doi.org/10.1007/s11845-008-0152-0
33. Tangkiatkumjai M, Boardman H, Praditpornsilpa K, Walker DM (2014) Reasons why Thai patients with chronic kidney disease use or do not use herbal and dietary supplements. BMC Complement Altern Med 14:473. https://doi.org/10.1186/1472-6882-14-473
34. Berg J, Morphew T, Tran J, Kilgore D, Galant SP (2016) Prevalence of complementary and alternative medicine usage in Vietnamese American asthmatic children. Clin Pediatr (Phila) 55:157–164. https://doi.org/10.1177/0009922815599394
35. Ozturk C, Karatas H, Längler A, Schütze T, Bailey R, Zuzak TJ (2014) Complementary and alternative medicine in pediatrics in Turkey. World J Pediatr 10:299–305. https://doi.org/10.1007/s12519-014-0507-8
36. Vinson R, Yeh G, Davis RB, Logan D (2014) Correlates of complementary and alternative medicine use in pediatric tertiary pain center. Acad Pediatr 14:491–496. https://doi.org/10.1016/j.acap.2014.04.003