Sider Honey Vs. Fluconazole and the Cure Rate of Vulvovaginal Candidiasis

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Abstract: Vulvovaginal candidiasis (VVC) is the most common gynecologic problems affecting 75% of sexually active women at least once in their life. It causes genital discomfort, loss of productivity, reduced sexual pleasure, and psychological distress.

Aim of the study: was to compare the effect of Sider honey VS. Fluconazole on the cure rate of Vulvovaginal candidiasis.

Methods: A quasi-experimental design was adopted.

Subjects: A total of 60 women were randomly recruited in the study; two groups were constituted 30 participants for each.

Setting: The study was conducted at Shaqra General Hospital and Al-anfal private hospital, at Shaqra governorate, the Kingdom of Saudi Arabia.

Tools: Two tools were developed and used by researchers to collect the data. A structured interview questionnaire included data related to demographic characteristics; medical history; and obstetric history and assessment tool to collect data related to self-reported symptoms before and after treatment and vaginal swab results. In addition, 5ml of Sider honey with a concentration of 80% was applied vaginally twice/day for 7 days.

Results: revealed that the mean age in women who applied Sider honey was 25.30 ± 5.02 years old. Eighty six point six percent of clinical cure rate and (76.7%) of mycological cure rate were observed in Sider honey group. In addition, self-reported symptoms were minimized in honey group than fluconazole group with statistical significant difference.

Conclusion: there is a highly statistical significance before and after applying diluted solution of Sider honey in relation to ; vaginal discharge, external vaginitis, non-menstrual bleeding, rash, vulvovaginal redness and Candida growth on Agar. Sider honey produced a high clinical cure rate and a reasonable mycological cure rate in women with VVC as compared to fluconazole.

Recommendations: Replication of the study on large sample selected from different geographical areas of Shaqra Cityto generalize the findings. Further research is needed to assess the efficacy of honey as an inhibitor of candida growth in clinical trials.

Key words: Vulvovaginal candidiasis (VVC), Sider honey, fluconazole

I. Introduction

Vaginal infection is one of the common causes of genital discomfort in women at reproductive age, and is the second reason for women to seek medical help from obstetrician after menstrual disorder (4). Vaginitis is characterized by a vaginal discharge, vulva itching and irritation. The three diseases commonly associated with vaginal discharge are bacterial vaginosisis (BV) (replacement of the normal vaginal flora by an overgrowth of anaerobic microorganisms, mycoplasmas, and Gardnerella vaginalis), trichomoniasis (T. vaginalis), and candidiasis (usually caused by Candida albicans) (1,2,3).

It was reported that about 75% of all females develop this infection at least once during their life; 90% of which are caused by Candida albicans. Ten to twenty percent of the affected women are asymptomatic; women are asymptomatic vaginal carriers; this infection may be increased by 40% during pregnancy(4). The annual cost of health care and lost productivity due to vulvovaginal candidiasis in the United States is estimated to be 1.8 billion, and is probable to reach 3.1 billion by 2014(5). It is believed that higher estrogen levels and higher glycogen content in vagina increases the risk of developing Vulvovaginal candidiasis(VVC) (6). Antibiotic and steroid therapies, oral contraceptive pills, diabetes mellitus, pregnancy, and immune-suppression were reported to increase the risk for the development of VVC(6).

Women with VVC usually complain of thick white caseous (curd-like) vaginal discharge and itching in addition to dyspareunia, vulva redness, and edema (6). It causes genital discomfort, loss of productivity, decrease sexual pleasure, and psychological distress. Honey according to Quran has great curing power against diseases.
So using of honey is a real glory treatment in Islam. According to Beretta, Caneva, Facino, evidence indicates that some varieties of honey contain kynurenic acid (a tryptophan metabolite with neuroactive activity) which may contribute to its antimicrobial properties. The presence of enzymes such as glucose oxidase, diastase, invertase, phosphatase, catalase and peroxidase has been found in honey that contributed to inhibit growth of candidiasis. There are several study report that honey is very effective as a dressing of wounds, burns, skin ulcers and inflammations; the anti-bacterial properties of honey speed up the growth of new tissue to help healing the wound and it is have variable broad-spectrum activities against different kinds of gram positive and enteric bacteria. Furthermore, laboratory studies and clinical trials have shown that honey is an effective broad-spectrum antimicrobial agent.

In addition, honey has been used since ancient times as part of traditional medicine. It also functions as an antibacterial, antioxidant, antitumor, anti-inflammatory, and antiviral. Honey is a drug in addition to its valuable nutrient contents. Honey was valued highly in the Middle East. It contains numerous compounds such as organic acids, proteins, amino acids, minerals, polyphenols, vitamins, and aroma compounds. It has been found to contain significant antioxidant activity including glucose oxidase, catalase, ascorbic acid, flavonoids, phenolic acids, carotenoid derivatives, organic acids, amino acids, and protein. Honey generates hydrogen peroxide when diluted because of the activation of the enzyme glucose oxidase, which oxidizes glucose to gluconic acid and hydrogen peroxide. Hydrogen peroxide is the major contributor to the antimicrobial activity of honey. Sider honey is considered the finest and the best quality around the world because the bee builds its hive without human interference, thus preserving its specification and its vital enzymatic constituents. Moreover, it possesses potent anti-inflammatory, antipyretic and analgesic properties which may be as a result of the phytochemicals present. The continuous elaboration of hydrogen peroxide from the honey through the glucose oxidase action is an additional factor. Although several in vitro studies have demonstrated the antibacterial activity of honey, limited number of studies have examined the activity of honey against fungi.

In a study by Al-Wailli, a mixture of honey, beeswax, and olive oil was effective in reducing the symptoms of dermatitis, and eradicated C. albicans from 50% of the culture-positive patients, during the seven-day trial. Moreover, in a study by Mercan et al., honey exhibited high anti-candidal activity on C. albicans, P. aeruginosa, E. coli, and S. aureus. Moreover, honey samples that were obtained from Izmir proved more effective as inhibitors against P. aeruginosa, E. coli, and S. aureus. The honey that was obtained from Muğla exhibited high anti-candidal activity on C. albicans. The nurse plays an active role as a health educator and counselor. She has to deliver important health educational instructions to the women such as personal hygiene, diet which increase immunity, and how to apply honey vaginally. Health professionals should perform careful assessment as observing signs and symptoms of vaginal Candidiasis, and presence of risk factors as being pregnant, passive smoking, antibiotics, immunosuppressive condition, diabetes mellitus, and improper personal hygiene. Health professionals who are caring for women during reproductive age and in health care settings should give them knowledge and increase their awareness, which consequently help them in improving their health by adopting preventive measures that help in reducing the incidence and avoid the complications of VVC.

Significance of the study
Recently, treatment of vaginal infection with the use of metronidazole or clindamycin administered orally or intravaginally is associated with poor initial cure rates in 10% to 15% of patients and recurrence rates of up to 80% in those who show initial response. The extensive use of azoles may effectively suppress Candida albicans but facilitate the overgrowth of non-albicans Candida. Furthermore, can cause several adverse effects as vomiting, diarrhea, abdominal pain, urination, pelvic cramps, dysmenorrhea, preteresthesia, rhinorrhea, headache and dizziness, fever, chills, vaginal burning, stinging, itching and irritation.

In Kingdom of Saudi Arabia, primary health care center is still lacking and there is gap in knowledge regarding incidence, causes and line of management of vaginal discharge. Also, through the clinical experience it was observed that Vaginal Candidiasis is one of the most common types of vaginal infection, and is the most common reasons for seeking medical care at the later stages of illness when the symptoms are aggravating. Vaginal Candidiasis causes genital discomfort, loss of productivity, reduced sexual pleasure, and psychological distress. Honey is one of the new antifungal strategies for treating VVC. In addition, there is a scattered research and low evidence based research that assess the effect of applying Sider honey in treating vaginal infection more specifically VVC. Therefore, the present study will add to the body of knowledge and evidence based regarding the use of honey as an alternative medicine strategy in treating vaginal infection compared to the standard routine care (fluconazole) in the treatment of VVC.

Aims of the study:
Was to compare the effect of Sider honey Vs. Fluconazole on the cure rate of Valvovaginal candidiasis.
**Research Hypotheses:**
To fulfill the aims of the current study the following research hypotheses are formulated

**H1.** Women with VVC who will apply Sider honey, will report less vaginal infection symptoms

**H2.** Women with VVC who will apply Sider honey will show a higher rate of cure than those who used antifungal medication (fluconazole).

**II. Subject and Methods**

**Research Design:**
A quasi-experimental design, pretest-posttest was used to achieve the aims of the study. In this design, data were collected from the participants both before and after applying Sider Honey.

**Setting:**
The study was conducted at Shaqra General Hospital and El-Anfal Private Hospital at Shaqra governorate in the Kingdom of Saudi Arabia (KSA). It is a university-affiliated Hospital which provides free health care to maternity as well as gynecological clients. Antenatal unit's clients are from all over Shaqra including upper and lower areas.

**Sample:**
A total of 60 women were randomly selected for the study. The inclusion criteria were women suffering from vaginal discharge associated with the following symptoms; itching, burning vaginal feeling, dyspareunia and dysuria, and vaginal sample were positive for Candida spp. Pregnant women with bacterial vaginosis or trichomoniasi, use of intravaginal antibiotics or antifungal agent were excluded. The sample was divided into two groups 30 for each. Group (A) is composed of the women who received Sider honey as the treatment of vulvovaginal candidiasis and group (B) is consisted of 30 women who received fluconazole (standard routine care).

Women were assigned randomly during the gynecological examination. The gynecologist collected two vaginal swabs from each subject suffering from the vaginal infection symptoms, swab which was labeled as odd number was the study group. One of the collected swabs were used for Gram stain and the other for isolation and identification of the Candida spp.

**Tools and measurements:**
To collect data pertinent to the study, three tools were constructed and used by the researcher after reviewing related literature. These are (1) A structured Interview questionnaire, (2) Assessment tool to assess symptoms of vaginal infection and follow-up, and (3) A mixture contained 80% honey and 20% distilled water.

1) **A Structured Interview Questionnaire**, included data related to personal background, medical history, and obstetric history. It was written in Arabic and simple language to be easy understood for all the participants.

2) **Assessment tool** include data related to symptoms of vaginal infection as follow up before and after applying Sider honey and vaginal swab result.

**Scoring System:**
Women response to the question regarding symptoms and risk factors of VVC were scored as (1) for correct answer and (0) for incorrect answer.

3) **A mixture that contained 80% honey and 20% distilled water.** The mixture was prepared by the researcher themselves and kept in sterile bottles.

**Tool validity and reliability:**

Tools were submitted to a panel of five experts in the field of Maternity Nursing and Obstetric Medicine to test the content validity. Modifications were carried out according to the panel judgment on clarity of the sentences and appropriateness of the content. Reliability test was assessed, $R=0.7$

**Pilot Study:**
A total of 10% of the study sample was included in the pilot study in order to assess the feasibility, clarity of the tool and determine time needed to answer the questions. It was excluded from the total sample.

**Ethical consideration:**
Each woman was informed about the purpose of the study and its importance. Researchers emphasized that participation in the study was entirely voluntary. Anonymity and confidentiality were also assured through coding the data. An informed written consent was obtained from the women who met the criteria of inclusion and accepted to be included in the study. All women were informed that they can withdraw any time from the
study without affecting their care and their data will be anonymous and be used only for the purpose of this study.

III. Procedures:

Before conducting the study, permission was obtained from the obstetric department in the previously mentioned settings followed by obtaining acceptance from the women to participate in the study. Ethical committee provided approval of the study and a written consent was obtained from all participant in advance. Data collection carried out through three phases: assessment, implementation, and evaluation phase.

1)-Assessment phase:
This phase included 2 sections: base line data was obtained from the women in both groups. Women were asked about their personal background data as age, educational level, marital status, residence and occupation. All of them were assessed for vaginal discharge. Medical history, physical examination and laboratory investigations were performed for women who were diagnosed as having vaginal infection.

2)-Isolation and identification of Candida species
The sample was collected by introducing a sterile non-lubricated speculum to the vagina; a cotton swab was then obtained from the vaginal discharge. The collected swabs for isolation and identification were introduced into tubes containing a 0.85% (w/v) sodium chloride solution and immediately transported to microbiology laboratory. A sterile non-lubricated vaginal speculum was introduced into the vagina and two cotton-swabs were obtained from the vaginal discharge. The first swab was smeared on a glass slide, left to dry at the room temperature then Gram stained and examined microscopically (1,000X magnification). The slide was examined for detection of Candida albicans (large oval gram positive budding cells).

The other swab was cultured on Sabouraud’s agar for the definitive diagnosis of Candida albicans. In culture, Candida albicans colonies appear as soft and creamy colored. All cultures were examined at least weekly for detection of the fungal growth and were kept for 6 weeks before being considered as negative.

2.A. Preparation of honey solutions
Honey solutions were prepared by diluting honey in Physiological saline (PBS, pH 7.2) to obtain 7 different concentrations (30%, 40%, 50%, 60%, 70%, 80% and 90% w/v). This step was used for all dilution steps under aseptic condition, According to the method described by (27).

<table>
<thead>
<tr>
<th>Honey concentration</th>
<th>sensitivity of C.albicans</th>
</tr>
</thead>
<tbody>
<tr>
<td>30</td>
<td>Resistant to honey</td>
</tr>
<tr>
<td>40</td>
<td>R</td>
</tr>
<tr>
<td>50</td>
<td>R</td>
</tr>
<tr>
<td>60</td>
<td>R</td>
</tr>
<tr>
<td>70</td>
<td>Sensitive to honey &amp; no growth</td>
</tr>
<tr>
<td>80</td>
<td>S &amp; no growth</td>
</tr>
<tr>
<td>90</td>
<td>S &amp; no growth</td>
</tr>
</tbody>
</table>

2.B. Minimum inhibitory concentration (MIC) determination
Concentration of each honey was incorporated into media to test their efficiency against C.albicans. Each plate with the lowest concentration of honey on which the strain not grow was considered as negative.

3)-Implementing phase:
This phase was applied to the study group only. The Sider honey was prepared by pouring the honey into a container having heated distilled water to 40°C and a sterile spoon was used for mixing to make the honey 80% diluted. The two materials were mixed thoroughly till making semi-liquid mixture. The mixture contained 80% honey and 20% distilled water. The mixture was prepared by the researcher themselves and kept in sterile bottles then given to the participants to be used at home. Women were instructed to use the mixture vaginally 5ml twice daily for 7 days. The mixture used in the study tested for its antifungal activities in culture media before using it clinically by the women. The result of therapy was initiated depending on the clinical diagnosis and the results of Gram stain without waiting for the results of the cultures. Written and oral instructions on self-care and the proper way for using the prepared solution was provided. The Written & oral instructions included the following: Proper technique of self-care: 1) Instruct women to wash her hands before and after each Perineal care, 2) Squeeze peri bottle (fill the bottle with cleaning warm water) or pour warm water or cleansing solution over perineum without separating the labia, 3) Instruct the woman how to pour the antiseptic solution over her Perineal area and ensuring that the solution flow is from the front to the back, 4) Dry the
Perineal area with dry tissue from front to back, and then discard it (disposal tissue preferable to prevent infection), 5) avoid moisture 6)-Apply the diluted solution of 5 ml Sider honey directly into vagina by using probe twice daily for one week.

Regarding the control group. The researchers dealt with each woman in control group during antenatal visit and the routine hospital care for vaginal infection (Fluconazole). Answering any question and the same baselines and following up assessments were conducted as those of the Sider honey.

4)-Evaluation phase:
In this phase, Follow-up visits were scheduled 1 week after treatment, at which the participants were interviewed for the presence of any side-effects, and asked about the presence of itching and/or discharge. Vaginal examination was done and two swabs from the vaginal discharge were obtained and evaluated using Gram staining as well as culture on to determine effectiveness of honey versus Fluconazole group.

Statistical Analysis
Statistical Package for Social Science (SPSS), version 16 was used for the analysis of the data. Collected data were coded and entered into computer. Data were examined for coding and entering error. Data were analyzed through inferential statistics which used to answer research questions. In this study, chi-square was used to compare between the categorical variables and differences between groups. Statistical significance was considered at p-value <0.05.

IV. Results
Findings of the current study are presented in three main parts: 1) description of the personal data and Anthropometrics measures of women; 2) the women’s predisposing factors for developing vaginal infection; and 3) symptoms of vaginal infection before and after applying Sider honey versus Fluconazole group.

1) Description of personal data and Anthropometrics measures of women
Regarding maternal age range, it was 19.48 years old with mean age 25.30 ± 5.02 years in the study group (A) who received Sider honey compared to 27.37 ± 7.33 in fluconazole group (B). Similar percentage in both group were married. In relation to educational level, about two third of the women in group (A) had high education compared to less than one third of the women in group (B) had secondary education. All women in group (A) were resident in urban area (100), compared to two third of group (B) (63.3%).

As regard Anthropometric measures two third of group (A) had normal weight compared to almost one third of group (B). Low percentages in both groups were over weight (Table, 1).

2) The women’s predisposing factors for developing vaginal infection:
Concerning predisposing factors for developing vaginal infection; high percentage in both group (40%) in group (A) compared to (43.3%) in group (B) were passive smoker. Low percentage in group (A) (6.67%) compared to (23.33%) in group (B) were pregnant (Table, 2).

3) Symptoms of vaginal infection before and after using sider honey.
As regard self-reported symptoms among both group. Table 3 revealed that there is a highly statistical significance difference between the two groups in relation to the self reported symptoms of rash and itching P=0.000. In relation to Sider honey treatments self-reported symptoms; Table (4) illustrated that there is a highly statistical significance difference was found before and after treatment by using diluted solution of Sider honey in relation to; vaginal discharge, external Vaginitis, non- menstrual bleeding, rash, vulvo- vaginal redness and Candida growth on Agar p=0.000, 0.01, 0.000, respectively.

| Table (1): Distribution of the Studied Sample Regarding Demographic Characteristics. |
|-----------------|-----------------|-----------------|
| | Group (A) | Group (B) |
| | (n=30) | (n=30) |
| Age (M±SD)yrs. Old | 25.30 ± 5.02 | 27.37 ± 7.33 |
| Educational level | | |
| Can’t read & write... | 2 (6.67) | 2 (6.67) |
| Read & write | 1 (3.33) | 3 (10) |
| Primary school | 3 (10) | 4 (13.33) |
| Secondary | 0 (0.0) | 10 (33.33) |
| University | 24 (80) | 11 (36.67) |
| Residence | | |
Table(2): Distribution of the studied group according to risk factors

<table>
<thead>
<tr>
<th>Variable</th>
<th>Group (A)(n=30)</th>
<th>Group (B)(n=30)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Sider Honey</td>
<td>Fluconazole</td>
</tr>
<tr>
<td></td>
<td>N</td>
<td>%</td>
</tr>
<tr>
<td>Passive smoker</td>
<td>12</td>
<td>(40)</td>
</tr>
<tr>
<td>Being pregnant</td>
<td>2</td>
<td>(6.67)</td>
</tr>
<tr>
<td>Family planning</td>
<td>9</td>
<td>(30)</td>
</tr>
<tr>
<td>Diabetes Mellitus</td>
<td>1</td>
<td>(3.33)</td>
</tr>
<tr>
<td>Anemia</td>
<td>5</td>
<td>(16.67)</td>
</tr>
</tbody>
</table>

Table (3): Distribution of symptoms of Vulvovaginal candidiasis among studied groups.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Group (A)(n=30)</th>
<th>Group (B)(n=30)</th>
<th>X2</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Sider Honey</td>
<td>Fluconazole</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>N</td>
<td>%</td>
<td>N</td>
<td>%</td>
</tr>
<tr>
<td>Vaginal discharge</td>
<td>25</td>
<td>(83.3)</td>
<td>19</td>
<td>(63.33)</td>
</tr>
<tr>
<td>External vaginal</td>
<td>20</td>
<td>(66.67)</td>
<td>18</td>
<td>(60)</td>
</tr>
<tr>
<td>Burning sensation</td>
<td>11</td>
<td>(36.67)</td>
<td>13</td>
<td>(43.33)</td>
</tr>
<tr>
<td>Non-menstrual bleeding</td>
<td>11</td>
<td>(36.67)</td>
<td>6</td>
<td>(20)</td>
</tr>
<tr>
<td>Rash</td>
<td>27</td>
<td>(90)</td>
<td>7</td>
<td>(23.33)</td>
</tr>
<tr>
<td>Itching</td>
<td>19</td>
<td>(63.33)</td>
<td>5</td>
<td>(16.66)</td>
</tr>
</tbody>
</table>

Fig.1. Culture of the vaginal discharge: On SDA Colonies are typically white to cream colored with a smooth, glabrous to waxy surface.

Fig.2. Evaluation the growth of Candida albican with different Sidr honey concentration show no growth in 90%, 80% and 70% concentration but show growth in 60% concentration.
**Table (4):** Distribution of the studied sample according to symptoms of vaginal infection before and after Application of Sider Honey

<table>
<thead>
<tr>
<th>Variable</th>
<th>Sider Honey (Group) (n=30)</th>
<th>Statistics</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>before application</td>
<td>After –Application</td>
</tr>
<tr>
<td></td>
<td>N</td>
<td>%</td>
</tr>
<tr>
<td>Vaginal discharge</td>
<td>25</td>
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<td>90</td>
</tr>
<tr>
<td>Itching</td>
<td>19</td>
<td>63.3</td>
</tr>
<tr>
<td>Vulvo-vaginal redness</td>
<td>20</td>
<td>66.7</td>
</tr>
<tr>
<td>Candida growth on Agar</td>
<td>28</td>
<td>93.3</td>
</tr>
<tr>
<td>Clinical cure rate</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Mycological cure rate</td>
<td>-</td>
<td></td>
</tr>
</tbody>
</table>

**Fig.3.** Clinical cure rate & Mycological cure rate among both groups

**Fig. 4.** Self-reported symptoms among both groups before and after treatment
V. Discussion

Vulvovaginal infection (VVC) affects an approximation of 70 to 75% of adult female, at least one episode occurs during the life. Sider honey is considered as the finest and the best in quality around the world for treat vaginal infection. Therefore, the current study is conducted to Was to compare the effect of Sider honey VS. Fluconazole on the cure rate of Vulvovaginal candidiasis. Findings of the current study are discussed within the following frame of references: 1) description of the personal data and Anthropometrics measures of women; 2) the women’s predisposing factors for developing vaginal infection; and 3) self-reported symptoms of infection among both groups, self-reported symptoms of infection before and after applying Sider honey.

Regarding socio-demographic characteristics age of the participant, in the current study it ranged from 19-48 years with a mean of 25.30 ± 5.02 years in group who received Sider honey compared to 27.37 ± 7.33 in fluconazole group. This finding was similar to that reported by Pirotta et al. who illustrated that risk factors for VVC included previous history of VVC, oral contraceptive pills, use of commercially available solutions for cleansing of external genitalia or vaginal douching, frequent sexual intercourse, sexual behavior (age at first intercourse,), contraception devices (diaphragm, vaginal contraceptive sponge, intrauterine device), and antibiotics. Furthermore, Younger women and those women with a history of bacterial vaginosis were at increased risk of vulvovaginal candidiasis episodes. Behavioral factors that were associated significantly with increasing vulvovaginal candidiasis recurrence ≥2-fold included wearing panty liners or panty hose and consuming cranberry juice or acidophilus-containing products.

Concerning the women’s predisposing factors for developing vaginal infection, in current study Potential risk factors for VVC included; being passive smoker, pregnancy, using contraceptive methods, diabetes mellitus and anemia. These findings is consistent with De Leon et al. who illustrated that risk factors for VVC included previous history of VVC, oral contraceptive pills, use of commercially available solutions for cleansing of external genitalia or vaginal douching, frequent sexual intercourse, sexual behavior (age at first intercourse,), contraception devices (diaphragm, vaginal contraceptive sponge, intrauterine device), and antibiotics. Furthermore, Younger women and those women with a history of bacterial vaginosis were at increased risk of vulvovaginal candidiasis episodes. Behavioral factors that were associated significantly with increasing vulvovaginal candidiasis recurrence ≥2-fold included wearing panty liners or panty hose and consuming cranberry juice or acidophilus-containing products.

Concerning self-reported symptoms before and after using Sider honey. The results revealed that self report vaginal infection as, vaginal discharge, external vaginitis burning sensation, non-menstrual bleeding and itching were improved after applying sider honey. With high percentage in clinical cure rate and mycological cure rate after applying honey for ten days with 80% diluted honey. Irish et al. reported antifungal efficacy of various honeys against clinical isolates of C. albicans C. glabrata and Candida dubliniensis. Khoisra et al. reported that honey has antifungal activity against Candida species such as Candida albicans, C. parapsilosis, C. tropicalis, Candida kefyr, C. glabrataandC. dubliniensis.

In the present study finding, diluted honey 80% more effective for minimized growth C. albicans with high clinical cure rate and reasonable mycological cure rate. Several studies have diluted honey with distilled water to obtain various volume/volume concentrations of honey. This findings is consistent with Banaeian-Borujeni et al. who mentioned that a concentration of 80% had the greatest inhibitory effect, whereas, higher and lower concentrations prevented the growth of Candida at the intermediate level.
Furthermore, honey had a high inhibitory effect at 80% concentration. Banaeian-Borujeni et al.; Koc et al.(36,17) illustrated that all honeys had antifungal activity at a high concentration of 80% (v/v), on fluconazole-resistant strains. A study by Al-Waili et al.,(22) reported that honey inhibited the growth of Candida at 30-100% concentration in Nutrient agar media. Furthermore, the inhibition of growth, but not killing has been reported in other studies(34). This may be related to sider honey generates hydrogen peroxide when diluted because of the activation of the enzyme glucose oxidase, which oxidizes glucose to gluconic acid and hydrogen peroxide is the major contributor to the antimicrobial activity of honey.

This result is contradictory with Al-Waili(22) who found that honey concentration ranging from 30% to 50% inhibits the growth of several pathogenic microorganisms, including C. albicans. Irish et al.,(33) reported that antifungal efficacy of various honeys against clinical isolates of C. albicans, Candida glabrata, and Candida dubliniensis. In the same line, Khosravi et al.,(34) mentioned that honey has antifungal activity against Candida species such as C. albicans, Candida parapsilosis, Candida tropicalis, Candida kefyr, Candida glabrata, and Candida dubliniensis.

VI. Conclusion and recommendation

In conclusion, the antifungal effect of Sider honey was evaluated in culture media containing different concentrations. Current study results revealed that Sider honey of 80% was effective in inhibiting the growth of C. albicans. There is a highly statistical significance difference between the women who applying sider honey as compared to fluconazole in relation to the self reported symptoms of vaginal infection. Moreover, there is highly statistical significance before and after treatment by using diluted solution of Sider honey in relation to vaginal discharge, external Vaginitis, non-mensual bleeding, rash, vulvo- vaginal redness and Candida growth on Agar. Sider honey produced a high clinical cure rate and a reasonable mycological cure rate in patients with VVC. Taken together, Honey appear to be useful and safe management of contained candidas, not only because of their effectiveness but also because of their safety, no adverse effects, which are often related to antifungal drugs (fluconazole).

Based on the study findings the following recommendations are suggested:

(1) - Further research is needed to assess the efficacy of honey as an inhibitor of candida growth in clinical trials.
(2) - Replicate the study with large sample size and different settings.
(3) - A cohort study about the effect of sider honey on treating various types of vaginal infection to provide research evidence related to the use of honey in complementary medicine.

Acknowledgment

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References

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