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Effect of *Sharbat-e-Deenar*in uncomplicated Pelvic Inflammatory Disease- A Clinical study

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ABSTRACT

Pelvic inflammatory disease (*Waram al-Rahim)*is one of the most serious gynaecological infections of the upper female genital tract with the world-wide annual rate of 10-20/1000 women of reproductive age. The objective planned for the study was to evaluate the effect of *Sharbat-e-Deenar* in uncomplicated Pelvic Inflammatory Disease (uPID). A pre and post observational single group clinical study was carried out in the Department of *IlmulQabalatwaAmrazeNiswan*, National Institute of Unani Medicine, Hospital, Bengaluru. Diagnosed cases (n=30) of uPID were included in the study. Patients with complicated PID, history of antibiotic therapy within seven days of recruitment; delivery, abortion or gynecologic surgery within the last 30 days, systemic diseases, malignancies, pregnancy & lactation were excluded. *Sharbat-e-Deenar*consists of *Poste baikhekasni*and*Tukhmekasni*(*Cichorium intybus* Linn.*), Gulesurkh (Rosa damascene* mill.*), Tukhmekasoos*(*Cuscutareflexa*Roxb.*)* and *Rewandchini (Rheum emodi*Wall. ex Meissn) were administered orally in a dose of 20 ml twice daily for 14 days. Outcome measures were 30-70% clinical improvement in Visual Analogue Scale (VAS) score for lower abdominal pain and McCormack Pain Scale (McPS) score for abdominopelvic tenderness and White Blood Cells (WBCs) count <10 on saline microscopy of discharge. Data were analyzed using paired Student 't' test, Wilcoxon Signed rank test and Paired Proportion test.Clinical improvement of 30-70% in McPS and VAS score was achieved in 96.7% (p<0.001**) and 93.3% (p<0.001**) patients respectively. WBCs count <10 on saline microscopy of discharge was achieved in 70% patients (p<0.001**).*Sharbat-e-Deenar*was effective in improving the sign & symptoms of PID due to its anti-microbial, anti-inflammatory, anti-spasmodic and anti-oxidant properties. No adverse effect of the research drug was encountered during the study. Hence, *Sharbat-e-Deenar* serves as an effective alternative in patients with PID, proving the research hypothesis.

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INTRODUCTION

Pelvic inflammatory disease (PID) is one of the major health issues adversely affecting reproductive-aged women as a consequence of STIs, worldwide with the annual rate of 10-20/1000 women of reproductive age (Sitnik and Levkovska, 2016). In classical Unani text, PID is referred as *waram al-Rahim,* which is classified into *waram al-rahim harr, waram al-rahimbalghami*and*waram al-rahimsawdawi.* The

uterus is usually affected by *waram harr* (acute inflammation) or *waramsulbsawdawi*(chronic inflammation), seldom with warambalghami (Khan and Akseer, 2011) involving either cervix uteri (Tib, 2010)or endometrium or fallopian tubes, ovaries and pelvic peritoneum (ZMA, 2001).Vast majority of women present with uPID are associated with too significant gynecological morbimortality, similar to complicated PID.PID occurs when microorganisms, such as *C. trachomatis, N. gonorrhea*, ascend from the lower to the upper genital tract. It has a polymicrobial etiology, and 70% of cases are nongonococcal and nonchlamydial including aerobic and anaerobic bacteria like *G. vaginalis, E. coli, Streptococcus* species etc (Judlin *et al.*, 2010).Women of younger age group and lower SES with early sexual exposure, multiple sexual partners, upper genital tract procedures or instrumentation are at increased risk of PID (Simms *et al.*, 2006). uPID is either clinically unapparent or with mild-to-moderate symptoms with no evidence of tubo-ovarian abscess and do not require parenteral treatment (Judlin *et al.*, 2010; Neto *et al.*, 2018). Patients of uPID presents with gradual, dull and bilateral lower abdominal pain and associated adnexal and/or cervical motion tenderness on bimanual examination, abnormal mucopurulent vaginal discharge, WBC $\geq$10/HPF on saline microscopy of discharge and/or CRP>6mg/l (Judlin *et al.*, 2010).Although conventional medicine used broad-spectrum antibiotics as a treatment option for PID, but their efficacy must be weighed against the possible side effects. Moreover, chances of antibiotic resistance and recurrence of disease after the stoppage of medicines is likely (Rahman *et al.*, 2014).Hence, there is an unmet need for safe & effective alternate treatment. *Sharbat-e-Deenar*possesses the properties of *musaffi-i-khun, mulatiff-i-khun, muhallil-i-waram, dafi'ta-affun, dafi'humma, mufarrih, munzij,* etc (Ghani, 2011; Kabeeruddin, 2006) and is beneficial in inflammation of viscera. The ingredients of *Sharbat-e-Deenar*, are *poste baikhekasni*and*tukhmekasni, gulesurkh, tukhmekasoos*and rewandchini (Kabeeruddin, 2006) which possesses *mudirr-i-bawl, mushil-i-safra, muqawwi-jigarwami'dawatihal*properties (Ghani, 2011), thus helpful in PID to get cured. Hence, *Sharbat-e-Deenar (Khan and Akseer, 2011; Kabeeruddin, 2006)*has been selected as a research drug in the study. Moreover, it's ingredients are pharmacologically proved to have anti-microbial, anti-inflammatory, anti-spasmodic, antioxidant, anti-pyretic, analgesic, sedative, anti-tumor, anti-HIV and hepatoprotective properties (Vijikumar *et al.*, 2011), attributing to their phytochemicals constituents such as alkaloids, inulin, coumarins, flavonoids, tannins, phenolic compounds, lactones, saponins (glycosides), carbohydrates, vitamins, minerals, volatile oils and steroids (Nwafor *et al.*, 2017).Thehypothesis tested was *Sharbat-e-Deenar* might be effective in the management of uPID and the objective planned for the study was to evaluate the effect of *Sharbat-e-Deenar*in uPID.

Methodology

Study design and setting

A pre and post observational single group clinical study was carried out in the Department of *IlmulQabalatwaAmrazeNiswan*, National Institute of Unani Medicine, Hospital, Bengaluru from Nov 2018-March 2019. The research protocol was approved by Institutional ethical committee prior to its commencement under IEC no. NIUM/IEC/2017-18/012/ANQ/04. The trial was registered at Clinical Trial Registry of India (CTRI) under the registration number CTRI/2018/03/012454.

Sample size estimation

Sample size was calculated for a single group with pre and post-assessment of the degree of pain with McPS. From the previous study, the mean of McPS was 10.5, with SD of 0.53 (Savaris *et al.*, 2007).The sample was calculated from the formula:n=2[(Z_α - Z_β)SD/μ_1-μ_2]$^{2.}$ It is validated from thumb rule for calculation of sample size, i.e. (SD/μ_1-μ_2)^2 $\times$20for 95% confidence limit. It was found to be 29.96~ 30. So, the sample size was fixed at 30 in the group.

Participants

Diagnosed cases (n=30) of uPID were included in the study. Patients with complicated PID, history of antibiotic therapy within seven days of recruitment; delivery, abortion or gynecologic surgery within the last 30 days, systemic diseases, malignancies, pregnancy &lactation were excluded. Laboratory investigations such as CBP, ESR, RBS, CUE, HIV, VDRL, abdominopelvic scan, Pap smear were done for exclusion.

Procedure

All women in the age group of 18-35 years attending Gynecology OPD of the Institute's Hospital fulfilling the inclusion criteria were invited to participate in the study. A thorough clinical history regarding age, socioeconomic status, menstruation, sexual exposure, obstetric outcome, contraception use and personal hygiene were enquired. The details of present complaints with duration in chronological order along with the history of similar complaints in the past and the treatment received were

recorded. The socioeconomic status and *mizaj* were assessed by Kuppuswamy's socioeconomic modified Scale and temperamental scale, respectively. Participants were instructed to empty the bladder prior to the gynecological examination. Abdominal palpation was carried out to assess the direct and rebound tenderness. VAS scale for pain and McPS of tenderness were used to assess the degree of pain and abdominopelvic tenderness, respectively. On P/S examination, the colour, consistency, amount and odour of vaginal discharge was elicited and under all aseptic precautions, a sample of vaginal discharge was taken for saline microscopy to look for the presence of WBCs/HPF. Bimanual examination was performed not only to assess the shape, size, position and mobility of uterus but also to assess the adnexal or cervical motion tenderness and to rule out any adnexal mass. All findings were documented in the case record form prepared for study. Participants were instructed to maintain personal hygiene, refrain from sexual intercourse or use barrier contraceptives and were not allowed to use any antibiotics and analgesic therapy during the study period. After systematic evaluation of patients with a clinical interview, they were subjected to necessary investigations such as AST, ALT, Alkaline phosphatase, Blood urea, Serum creatinine, CRP and Wet mount test.

Intervention

*SharbatDeenar*was prepared in NIUM pharmacy as per the method mentioned in classical Unani text. All drugs, including *Tukhmekasoos* (*ba surra basta)*, were soaked in water which was six times of drugs for 24 hours, except *Rewandchini*. Dry *Rewandchini* was added in powder form while preparing decoction, which was filtered and then mixed with sugar to formulate *qiwam*. Test drug was administered orally in a dose of 20 ml twice daily for 14 days (Kabeeruddin, 2006).Each participant was provided with 300 ml of test drug in plastic bottles on 1^{st} visit for seven days and was instructed to receive rest of the drug on 2^{nd} visit for the remaining 7 days. To ensure blinding the test drug was dispensed in unlabeled plastic bottles. To confirm the compliance to treatment, medicine was given for 7 days only and was instructed to visit on subsequent follow up with empty bottles to receive the rest of the treatment.

Subjective parameters

Lower abdominal pain &low backache (Judlin *et al.*, 2010; Savaris *et al.*, 2007) was recorded on3 pointer scale (mild-1, moderate-2andsevere-3) and abnormal vaginal discharge was recorded according to the severity as grade 1-Mild (without staining or moistening of underclothes), grade 2-Moderate (underclothes are wet and require changing) and grade 3-Severe (requires the wearing of the extra-absorbent pad) (Sayed *et al.*, 2016).

Objective parameters

Visual analogue scale (VAS) for lower abdominal pain

The intensity of pain was objectively assessed by a colored visual analogue scale. It is a 10 cm straight line with anchors placed at both the ends (0 indicate no symptoms and 10 indicate worst possible pain). Before pelvic examination, patients were asked to place a mark somewhere along the line that best described the actual status of their symptoms (Judlin *et al.*, 2010; Savaris *et al.*, 2007; Sayed *et al.*, 2016).

McCormack pain scale for abdominopelvic tenderness

It is four-pointer tenderness scale which assess direct and rebound tenderness and ranges from 0 to 3, (0=tenderness absent,1=tenderness referred by the patient, 2=tenderness causing observable distress, 3=rebound tenderness). Total score was defined as the sum of individual scores for 12 abdominal and pelvic regions (maximum score =36) (Sayed *et al.*, 2016).

WBCs on HPF

Under all aseptic precautions, a sample of vaginal discharge was taken with a spatula from ectocervix and placed on a clean glass slide and 1-2 drops of normal saline was added to make a thin film, covered with a sterile coverslip and observed under a microscope for the presence of no of white blood cells/HPF. WBCs $\geq$10/HPF is suggestive of leucorrhoea.

C-reactive protein (CRP)

Blood sample for CRP were collected before and after the intervention (Savaris *et al.*, 2007). CRP is an inflammatory marker to support the diagnosis of PID, often normal in mild/moderate PID and CRP <3.0 mg/l is considered as normal.

Outcome measures

Clinical improvement inMcPS score of 30-70%, VAS score of 30-70% and WBCs count <10/HPF on saline microscopy of discharge (Judlin *et al.*, 2010; Savaris *et al.*, 2007).

Adverse effect documentation

No adverse effects of research drug were encountered during the study period as a safety profile were within normal limits.

Statistical Methods

Descriptive and inferential statistical analysis has been carried out in the present study. Results on continuous measurements are presented on Mean ± SD (Min-Max) and results on categorical measurements are presented in Number (%). Significance is assessed at 5% level of significance. Student t-test (two-tailed, dependent) has been used to find the significance of study parameters on a continuous scale within each group. The Statistical software, namely SPSS 22.0, and R environment ver.3.2.2 were used for the analysis of the data and Microsoft Word and Excel have been used to generate graphs, tables etc.

RESULTS AND DISCUSSION

A total of 129 patients were screened for the study, 47 denied and 82 were willing to participate. 11 out of 82 patients did not fulfil the diagnostic criteria (not ready for bimanual examination) and 7 patients withdrew the consent. Sixty-four patients were subjected to investigations; 34 were excluded for not meeting the inclusion criteria and 30 were included in the study, 28 patients completed the trial & 2 patients were lost to follow up (inability to come on a subsequent visit), but included in the final analysis by last observation carried forward method.

Main findings

The present study confirmed that clinical improvement of 30-70% in McPS and VAS score was achieved in 96.7% ($p<0.001^{**}$) and 93.3% ($p<0.001^{**}$) patients respectively. WBCs count <10 on saline microscopy of discharge was achieved in 70% patients ($p<0.001^{**}$).

Baseline characteristics

Age

50% of patients were in the age group of 20-30 years & remaining 43.3% and 6.7% were in 31-40 and <20 years of age respectively. Higher prevalence of PID in women between 20-30 years of age is in accordance with the findings of Eze JC. *et al. (Eze et al., 2018)*as this is the sexually active group. Mean age of patients was 28.23±4.97, which is in accordance with the study of Sayed A. *et al. (Sayed et al., 2016)* reported 27.65± 4.48 & 27.2± 4.84, Savaris RF.*et al (Savaris et al., 2007)*reported 28.3±0.8 and 29.3±1.1yrs, in two groups.

Socioeconomic status

In this study, most of the patients were from middle socioeconomic class (40% upper middle class & 36.7% lower middle class); while, 16.7% and 6.7 % were from upper lower & upper class, respectively.

Marital status

In this study, 100% of women suffering from PID were married, which is in agreement with the studies of Ahmed S.*et al (Ahmed et al., 2017) and* ShindeSA.*et al, (SA et al., 2018)*who reported PID in 90% married women.

Contraception history

In this study, 46.7% of patients were tubectomised, 36.7% were non-contraceptive users, 13.3% were using barrier methods and 3.3% used oral contraceptive pills. As a majority of patients were multipara, so they opted for sterilization.

Number of live births & abortion

Majority of PID patients(66.6%) had parity between 2-5; 16.7% had parity one and similar % of women were nulliparous, which is accordance with the studies of Ahmed S.*et al (Ahmed et al., 2017)* and Shinde SA.*et al, (SA et al., 2018)* who reported incidence of PID between 2-5 parity in 56% and 58% patients respectively.

Viral markers

Serology for VDRL & HIV was non-reactive in 100% of patients. In a teenage group, STD-related PID is more common in developed countries, while anaerobic bacterial colonization is probably the major reason of PID in women of a higher aged group in developingcountries (Ahmed *et al.*, 2017).

Pap smear

In 56.7% of patients, pap smear showed inflammatory smear, 30.0% had acterial vaginosis and 13.3% had a normal smear.

Mizaj

46.7% patients possessed *balghamimizaj,* 26.7% had *damwimizaj,* 20% were*safrawi*and 6.7% had*sawdawimizaj.* It is contradictory to the opinion of Unani scholars regarding the pathophysiology of a disease that this disease is common in *harr mizaj* individual (Khan and Akseer, 2011).

Pelvic Ultrasonography

66.7% of patients had a normal pelvic scan, though 33.3% had pelvic inflammatory disease. This may be due to the stage of infection at the point of diagnosis (Table 1).

Subjective Parameters

Lower abdominal pain

At baseline, lower abdominal pain was mild & moderate in 36.7% & 63.3% patients, respectively and after treatment, it was reduced to 6.7% & 3.3% patients, respectively with an improvement of 90% which matched with the study of Sayed A.*et al. (Sayed et al., 2016).* At baseline, mean±SD was

Table 1: Baseline characteristics

Baseline characteristics		No. of patients	%
Risk factors			
Age in years	<20	2	6.7
Mean±SD 28.23±4.97	20-30	15	50.0
	31-40	13	43.3
Socio-Economic Status	Lower Middle	11	36.7
	Upper	2	6.7
	Upper Lower	5	16.7
	Upper Middle	12	40.0
Marital Status	Married	30	100.0
	Single	0	0.0
H/o Contraception	Absent	11	36.7
	Barrier Contraception	4	13.3
	Oral Contraceptive Pills	1	3.3
	Tubectomized	14	46.7
Live Birth	0	5	16.7
	1	5	16.7
	2	11	36.7
	3	8	26.7
	5	1	3.3
Abortion	Nil	24	80.0
	1	6	20.0
HIV and VDRL	Non-reactive	30	100.0
	Reactive	0	0.0
Pap smear	Normal smear	4	13.3
	Bacterial Vaginosis	9	30.0
	Inflammatory smear	17	56.7
Mizaj	*Balghami*	14	46.7
	Damwi	8	26.7
	Safrawi	6	20.0
	Sawdawi	2	6.7
BMI (Kg/m^2)	<18.5	3	10.0
Mean±SD 26.03±6.40	18.5-25	11	36.7
	25-30	9	30.0
	>30	7	23.3
Abdominopelvic Scan	NAD	20	66.7
	Yes	10	33.3
	Cervicitis	1	3.3
	Endometritis	1	3.3
	PID	8	26.7

Data were presented as number (percentage),Student t-test (two-tailed, dependent)

Table 2: Effect of Research Drug on Lower abdominal pain (LAP)

LAP	BT	During Treatment		After Treatment		% difference
		1^{st}FU	2^{nd}FU	1^{st}FU	2^{nd}FU	
0 (Absent)	0(0%)	3(10%)	24(80%)	26(86.7%)	27(90%)	90.0%
1 (Mild)	11(36.7%)	23(76.7%)	6(20%)	4(13.3%)	2(6.7%)	-30.0%
2 (Moderate)	19(63.3%)	4(13.3%)	0(0%)	0(0%)	1(3.3%)	-60.0%
Mean±SD	1.63±0.49	1.03±0.49 <0.001**	0.20±0.41 <0.001**	0.13±0.35 <0.001**	0.13±0.43 <0.001**	-

Data were presented as number (percentage) and mean ±SD, LAP improved to 90%

Table 3: Effect of Research Drug on White discharge per vaginum (WDPV)

WDPV	BT	During Treatment		After Treatment		% difference
		1^{st} FU	2^{nd} FU	1^{st} FU	2^{nd} FU	
0 (Absent)	0(0%)	0(0%)	4(13.3%)	9(30%)	10(33.3%)	33.3%
1 (Mild)	3(10%)	14(46.7%)	24(80%)	19(63.3%)	17(56.7%)	46.7%
2 (Moderate)	25(83.3%)	14(46.7%)	2(6.7%)	2(6.7%)	3(10%)	-73.3%
3 (Severe)	2(6.7%)	2(6.7%)	0(0%)	0(0%)	0(0%)	-6.7%
Mean±SD	1.97±0.41	1.60±0.62 <0.001**	0.93±0.45 <0.001**	0.77±0.57 <0.001**	0.77±0.63 <0.001**	-

Data were presented as number (percentage) and mean ±SD, WDPV improved to 80.0%

Table 4: Effect of Research Drug on Low backache

Low backach	BT	During Treatment		After Treatment		% difference
		1^{st} FU	2^{nd} FU	1^{st} FU	2^{nd} FU	
0 (Absent)	0(0%)	1(3.3%)	2(6.7%)	5(16.7%)	6(20%)	20.0%
1 (Mild)	15(50%)	18(60%)	20(66.7%)	17(56.7%)	16(53.3%)	3.3%
2 (Moderate)	15(50%)	11(36.7%)	8(26.7%)	8(26.7%)	8(26.7%)	-23.3%
Mean±SD	1.50±0.51	1.33±0.55 0.025*	1.20±0.55 0.007**	1.10±0.66 0.006**	1.07±0.69 <0.001**	-

Data were presented as number (percentage)&mean±SD, Low backache improved to 23.3%

Table 5: Effect of Research Drug on VAS score for lower abdominal pain (LAP)

VAS score for	BT	During Treatment		After Treatment		% difference
		1^{st} FU	2^{nd} FU	1^{st} FU	2^{nd} FU	
0	0(0%)	3(10%)	22(73.3%)	26(86.7%)	27(90%)	90.0%
1	0(0%)	2(6.7%)	5(16.7%)	2(6.7%)	1(3.3%)	3.3%
2	1(3.3%)	11(36.7%)	2(6.7%)	1(3.3%)	0(0%)	-3.3%
3	15(50%)	8(26.7%)	1(3.3%)	1(3.3%)	2(6.7%)	-43.3%
4	13(43.3%)	6(20%)	0(0%)	0(0%)	0(0%)	-43.3%
5	1(3.3%)	0(0%)	0(0%)	0(0%)	0(0%)	-3.3%
Mean ± SD	3.47±0.63	2.40±1.19 <0.001**	0.40±0.77 <0.001**	0.23±0.68 <0.001**	0.23±0.77 <0.001**	-

Data were presented asnumber (percentage) and mean ±SD, VAS score improved to 93.3%

Table 6: Effect of Research Drug on McPSsubscore for Abdominal Tenderness (abd.tds.)

McPSsubscore for a	BT	During Treatment		After Treatment		% difference
		1^{st} FU	2^{nd} FU	1^{st} FU	2^{nd} FU	
0	0(0%)	0(0%)	16(53.3%)	23(76.7%)	24(80%)	80.0%
1-3	6(20%)	18(60%)	13(43.3%)	6(20%)	5(16.7%)	-3.3%
4-6	20(66.7%)	10(33.3%)	1(3.3%)	1(3.3%)	1(3.3%)	-63.4%
7-10	4(13.3%)	2(6.7%)	0(0%)	0(0%)	0(0%)	-13.3%
Mean ±SD	4.63±1.43	3.50±1.55	1.00±1.26	0.57±1.19	0.50±1.17	-
		<0.001**	<0.001**	0.001**	<0.001**	

Data were presented as number (percentage) and mean±SD, McPSsubscore for abd.tds. improved to 80%

Table 7: Effect of Research Drug on McPSsubscore for pelvic tenderness (pel.tds.)

McPSsubscore for l	BT	During Treatment		After Treatment		% difference
		1^{st} FU	2^{nd} FU	1^{st} FU	2^{nd} FU	
0	0(0%)	2(6.7%)	13(43.3%)	17(56.7%)	19(63.3%)	63.3%
1	1(3.3%)	8(26.7%)	12(40%)	9(30%)	7(23.3%)	20.0%
2	16(53.3%)	14(46.7%)	5(16.7%)	4(13.3%)	4(13.3%)	-40.0%
3	9(30%)	4(13.3%)	0(0%)	0(0%)	0(0%)	-30.0%
4	4(13.3%)	2(6.7%)	0(0%)	0(0%)	0(0%)	-13.3%
Mean ± SD	2.53±0.78	1.87±0.97	0.73±0.74	0.57±0.73	0.50±0.73	-
		<0.001**	<0.001**	<0.001**	<0.001**	

Data were presented as number (percentage), mean±SD, McPSsubscore for pel.tds. improved to 83.3%

Table 8: Effect of Research Drug on WBCs/HPF

WBCs /HPF	BT	During treatment		After treatment	
		1^{st} FU	2^{nd} FU	1^{st} FU	2^{nd} FU
Mean ± SD	58.33±31.77	41.13±26.85	22.10±24.04	15.87±23.71	16.07±24.35
difference	-	17.200	36.233	-	42.267
p-value	-	<0.001**	<0.001**	-	<0.001**

Table 9: Effect of Research Drug on CRP

Parameter	BT	AT	Difference	p-value
CRP (mg/l)	4.17±4.18	3.07±1.95	1.104	0.182

Table 10: Effect of Research Drug on Safety Profile

Safety profile	BT	AT	difference	P-value
Liver Function Test				
AST (IU/L)	25.21±9.28	28.59±11.49	-3.382	0.228
ALT (IU/L)	23.95±9.17	23.38±9.35	0.570	0.816
Alkaline Phosphate (IU/L)	182.13±51.11	200.72±50.76	-18.590	0.074+
Renal Function Test				
Blood Urea (mg/dl)	25.16±6.42	24.96±5.24	0.200	0.885
Serum Creatinine (mg/dl)	0.79±0.16	0.86±0.16	-0.064	0.082+

Data were presented as mean±SD, Student t-test

Table 11: Effect of Research Drug on outcome measures

Outcome measures		No. of patients (n=30)	%
30-70% Improvement			
McPS score	No	1	3.3
	Yes	29	96.7
VAS score	No	2	6.7
	Yes	28	93.3
WBCs<10/HPF			
No		9	30.0
Yes		21	70.0

Data were presented as number (percentage)

1.63±0.49 which was reduced to 0.13±0.43 after treatment with p-value <0.001, considered as highly significant (Table 2).

Vaginal discharge

At baseline, the vaginal discharge was mild, moderate & severe in 10%, 83.3% & 6.7% patients respectively, which was improved to no discharge in 33.3%, mild in 56.7%, moderate in 10% patients and no patient had severe vaginal discharge after treatment, with the improvement of 80%. Sayed A.*et al (Sayed et al., 2016)* reported mild, moderate & severe vaginal discharge in 5%, 90%, 5% patients before treatment which was improved in 90%, 10%, 0% respectively after treatment & improvement in vaginal discharge was higher in the present study as compared to this study. At baseline, mean±SD was 1.97±0.41 which was reduced to 0.77±0.63 after treatment with p <0.001 (SS),which is consistent with the study by Zahid S.*et al (Zahid and Rehman, 2016)*reported 1.73±0.45 and 0.30±0.47 before & after treatment (Table 3).

Low backache

At baseline, low backache was mild & moderate in each 50% patients, which was improved in 23.3% patients after treatment with p = 0.079+ suggestive significant. Sayed A.*et al (Sayed et al., 2016)*reported improvement in 35% and 40% patients in two groups. At baseline, mean±SD of low backache was 1.50±0.51, which was reduced to 1.07±0.69 after treatment with p <0.001 (SS) (Table 4).

Objective Parameters

VAS score for lower abdominal pain

At baseline, in the majority of cases VAS score was 3 & 4 in 50% and 43.3% patients respectively, which was improved to score 0 & score 3 in 90% & 6.7% patients respectively after treatment, with an overall improvement of 93.3%. At baseline, mean± SD was 3.47±0.63 which was reduced to 0.23±0.77 after treatment with p <0.001(SS), which is in accordance with the study of Sayed A. *et al. (Sayed et al., 2016)*reported 4.45±0.51 and 0.15±0.63 respectively before & after treatment (Table 5).

McPS score for abdominal and pelvic tenderness

At baseline, McPSsubscore (for abdominal tenderness) was ranging from 1-3, 4-6, 7-10 in 20%, 66.7%, 13.3% patients, which was reduced to 16.7%, 3.3%, 0%, respectively after treatment with an improvement of 80%. McPSsubscore (for pelvic tenderness) was ranging from 1, 2, 3 & 4 in 3.3%, 53.3%, 30% & 13.3% patients which was reduced after treatment to 23.3%, 13.3%, 0% & 0%, respectively with an improvement of 83.3%. Mean±SD of McPSsubscore for abdominal and pelvic tenderness at baseline, 1^{st} & 2^{nd} follow up, during & after treatment was 4.63±1.43, 3.50±1.55, 1.00±1.26, 0.57±1.19, 0.50±1.17, and 2.53±0.78, 1.87±0.97, 0.73±0.74, 0.57±0.73, 0.50±0.73, respectively withp<0.001**(SS). Before & after treatment, the mean total pain score was 7.16±2.16 and 1.00±1.90, respectively, which is in accordance with the study of Sayed A.*et al (Sayed et al., 2016)*reported mean±SD of total pain score and pelvic subscore of 8.2±1.47 &4.85±0.99 and 2.05±1.79 & 1.35±1.3, respectively (Tables 6 and 7).

White Blood Cells /HPF

At baseline, mean±SDof WBCs/HPF was 58.33±31.77, which was reduced to 16.07±24.35 after treatment, with p <0.001(SS). Zahid S.*et al (Zahid and Rehman, 2016)*reported mean±SD of WBCs/HPF of 26.07±9.35 and 4.57±4.79 before and after treatment (Table 8).

CRP

Mean±SD of CRP before and after treatment was 4.17±4.18 and 3.07±1.95, respectively, with p-value =0.182 (NS). Though CRP supports the diagnosis of PID, it is nonspecific and often normal in mild/moderate PID (Vijikumar *et al.*, 2011)

(Table 9).

Safety and tolerability

Sharbat-e-Deenar was proved to be safe as all safety parameters were within normal limits, except alkaline phosphatase (p =0.074+) and serum creatinine (p =0.082+) in which significant suggestive changes were observed during the trial (though both values are within normal range only) and no serious adverse effects were encountered during the study period, thus validating the safety of research drug. 100% compliance was achieved with the research drug due to its palatable taste (Table 10).

Outcome measures

The present study confirmed that clinical improvement of 30-70% in McPS and VAS score was achieved in 96.7% and 93.3% patients, respectively and WBCs count <10 on saline microscopy of discharge was achieved in 70% patients. Reduction of the pain criterion in McPS& VAS reported by Judlin P.*et al (Judlin et al., 2010)*91.4% & 86.8%, Sayed A. *et al (Sayed et al., 2016)*75% & 90%, Asicioglu O.*et al (Asicioglu et al., 2013)*82.7% & 79.5%, respectively. Results of all these studies matched with the present study. Hence, marked improvement in outcome measures was observed with just 14 days of intervention. *Sharbat-e-Deenar*possess *dafi-i-ta'ffun, musaffi-khun, muhallil-i-awram, dafi-i-sayalan-al-rahim, dafihiddatekhunwasafra, musakkin, muqawwianda-roonea'da, tanqiyaakhlat*properties (Ghani, 2011); which probably might resolve the inflammation, relieve pain and improve general vitality. Moreover, pharmacological studies confirmed that constituents of *Sharbat-e-Deenar*contains phytochemicals such as alkaloids, inulin, coumarins, flavonoids, tannins, phenolic compounds, lactones, saponins (glycosides), carbohydrates, vitamins, minerals, and volatile oils and steroids,which have demonstrated for biological activities such as antimicrobial, anti-inflammatory, antioxidant, antispasmodic, anti-pyretic, analgesic, sedative, anti-HIV, antiparasitic, anticancer, hepatoprotective etc (Nwafor *et al.*, 2017).These active compounds probably inhibits the synthesis and release of inflammatory mediators, therefore inhibiting the inflammatory response (Malik *et al.*, 2010) (Table 11).

Strength

This study is first of its kind to report the effect of *Sharbat-e-Deenar* in uPID. In a population that has erratic healthcare-seeking behaviour, poor treatment compliance with other Unani drugs, *Sharbat-e-Deenar* may be the better treatment of choice.

Limitation

Sample size was too small to draw conclusions based on data. The short duration of intervention, short follow up, more specific investigations like cervical swab PCR culture and NAAT to identify the causative organism was not done during the study. These limitations emphasize the need for future research.

CONCLUSIONS

Finally, it can be inferred that *Sharbat-e-Deenar* was effective in abolishing inflammation, associated tenderness, relieving symptoms and improving the general condition in patients with uPID. No adverse effects were noted during the trial. Hence, *Sharbat-e-Deenar* serves as an effective alternative in patients with uPID.

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Conflict of Interest

The authors declare that they have no conflict of interest for this study.

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