

“Clinical study and therapeutic response of some unani drugs in cases of *iltehab-e-mahbal* with special reference to *Candida albicans*”

Dr Nazia shamshad¹, Dr. S.A.Naaz², Prof. Q.A. Kazmi³

¹Medical Officer at University college of Unani Tonk, Constituent college of, Dr. S.R. Rajasthan Ayurved university, Jodhpur, (Raj).

²Chairman Dept. of Qabalat Wa Niswan AKTC.AMU, Aligarh.

³Former Chairman Dept. of Qabalat Wa Niswan AKTC.AMU, Aligarh.

INTRODUCTION

Iltehab-e-mahbal or vaginitis is the inflammatory or infectious condition of vaginal mucosa, it can results into vulvovaginal symptoms such as itching, burning, irritation and abnormal vaginal discharge (2,39,43). Vaginitis is a debilitating condition, it accounts for more than an estimated 10million physician office visit annually. In 1849 Wilkinson recorded the first description of vulvovaginal candidiasis and its treatment with hypochlorite solution. An estimated 75% women experiences at least one episode of Candidial vaginitis (VVC) during their lifetime and 45% have two or more episodes (03,08,12,33,47). It is one of the common cause of infective vaginal discharge in the women of reproductive age group and one of the most common reasons for patient's frequent visits to gynaecologist (15). It is caused by a fungus known as *Candida* having multiple species but 90% cases are caused by *candida albicans* (fitre abyaz) (07,14,25,37,44). Women find this disease as a source of discomfort, inconvenience, decreased libido, loss of productivity and psychological distress. It is associated with other infections of female genital tract and often causes PID and infertility. Risk factors include use of oral contraceptive pills (OCPs), antibiotics (20) pregnancy, gestational diabetes, women with the diagnosis of AIDS and douching etc. Its complications are vulvar vestibulitis Syndrome and chorioamnionitis in pregnancy (06,08,32,38).

In classical literature of Unani medicine clinical features of candidial vulvo-vaginitis are mentioned under the head of *Sailan-ur-Rehm*. In unani literature it was mentioned that, all the discharges coming from genital tract including rehm (uterus), unqur rehm (cervix) and mahbal (vagina) other than blood, are described under the head of *Sailan-ur-Rehm*. According to eminent unani physician it is cause by *zoaf-e-ghazia* of rehm (defect in nutritive faculty of uterus) , accumulation of *fuzulat* (waste product) in the body and *ghalba* of any one of *akhklat-e-arba* (predominance of humours) (04,05,21,23,27).

A wide variety of medical therapy is available today for the treatment of candida vaginitis but no treatment promises complete cure. On the contrary patients develop the risk of pelvic inflammatory disease, Infertility and other infections reproductive organs. The modern medicines like oral fluconazole of 150mg (25,45) have been approved for the treatment of CVV but these drugs has been reported to develop resistance and produce side effects and recurrence rate is also high. So the eyes are on traditional system of medicine for the treatment of this disease which is cost effective and develops minimum side effect with low recurrence rate. Such an approach has the potential to reduce the overall cost of cure while maintaining efficacy and overall patient's satisfaction.

MATERIAL AND METHODS

The prospective randomized clinical study was conducted in the Outpatient Department (OPD) and (IPD) In patient Department of Qabalat-wa- Niswan, Ajmal Khan Tibbiya College Hospital, Aligarh Muslim University, Aligarh from December 2009 to May 2011. The study protocol was approved by the members of Board of Studies during the year 2007-08 and the study took about 1½ years to complete. Patients signed the consent form before taking part in the study. The details of study, treatment strategies and purpose of study were explained in detail to the patients and no subject underwent any kind of examination and investigation before giving written consent.

Inclusion Criteria:

- ✓ Married women complaining of thick curdy white discharge per vaginum with itching vulva, dyspareunia, dysurea, low-backache, burning micturition.

- ✓ Reproductive age group.
- ✓ Reddened vaginal wall.
- ✓ Given consent voluntarily.

Exclusion Criteria:

- ✓ White discharge per vaginum without itching.
- ✓ Pregnant women.
- ✓ Diagnosed cases of AIDS, TB, Syphilis, Gonorrhoea, Trichomoniasis and bacterial vaginosis.
- ✓ Diagnosed cases of Diabetes mellitus.
- ✓ Diagnosed cases of carcinoma.

Subject:

We screened total 80 patients with white discharge per vaginum. KOH mount microscopy of discharge showed fungal element in 50 cases while remaining 30 were negative for fungal element. Out of these 50 cases PAP smear was done in 30 cases and fungal culture in 5 cases.

Procedure:

All women attending OPD of Qabalat-wa-Niswan were interrogated whether they had complaint of discharge per vaginum or not. The 50 patients underwent thorough history taking, physical examination including p/s and p/v examination to confirm the diagnosis of Candida vaginitis. Routine investigations were carried out.

A detail clinical history was taken using a standardized performa with particulars about, name, age, address, contact number, education, socio-economic status, religion and presenting complaints in chronological order for which she sought advised from gynaecologist.

Parameters for evaluation of efficacy of trial drug:

1. Subjective parameters: It includes symptoms, white discharge, itching vulva, LBA, Pain in Lower abdomen, Dysuria, Dyspareunia.
2. Objective parameters: By KOH mount microscopy to detect presence or absence of mycelia of fungus for VVC. Final Statistical analysis was performed after completion of 50 cases.

Unani Drugs used in the Trial:

For the rational and effectual Management of this ailment, a Unani formulation was required which could revert this pathology to normalcy. By careful forage of Unani Literature the following Unani drugs have all requisite properties like *Habis* (Styptic), *Qabis* (Astringent), *Mujaffif* (Desiccative), *Musaffiyat* (Purifier) *dafetaffun*, Antibacterial, Anti inflammatory, Antifungal etc. to which they stop the growth of micro-organisms thus preventing the source of discharge (09,28,34,40,41,42,46,). The six drugs selected for trial are namely:

<i>Mako</i>	<i>(Solanum nigrum)</i>
<i>Kasni</i>	<i>(Cichorium intybus)</i>
<i>Dar-e-hald</i>	<i>(Berberis aristata)</i>
<i>Baboona</i>	<i>(Matricaria chamomilla)</i>
<i>Suhaga</i>	<i>(Borax)</i>
<i>Satawar</i>	<i>(Asparagus racemosus willd)</i>

METHOD OF PREPARATION

They are divided into two groups on the basis of route of Administration. *Aab-e-mako* and *kasni* collectively known as *Aab-e-Murawwaqain* given orally in the dose of 25 ml trice a day for 14 days.

Remaining four drugs i.e. *Baboona*, *Suhaga*, *Satawar* and *Dar-e-Hald* all are in equal proportion given locally in the form of vaginal tablet of 1 gm each to be kept overnight in vagina for 14 consecutive night. *Samagh-e-Arbi* is used as a medium to bind the vaginal tablet.

A vaginal tablet of 1gm was prepared to be kept overnight in vagina for 14 consecutive nights. Along with *Aab-e-Murawwaqain* was given orally 25 ml twice a day for 14 days and follow up was done at each cycle for 3 consecutive cycles. No any other concomitant treatment is allowed during the trail therapy. The

subjective parameters as basal clinical symptoms and objective parameters as basal microscopic findings were recorded. Microscopic examination was performed after completion of therapy to assess the cure.

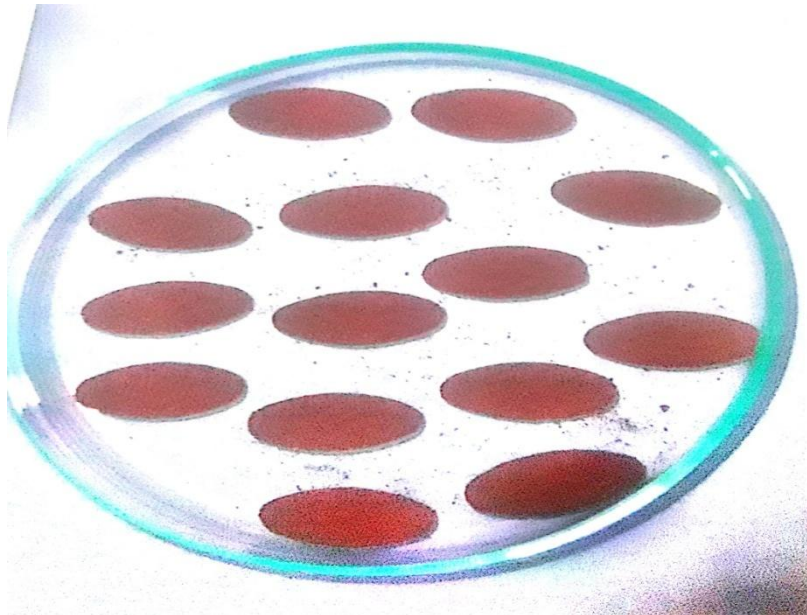


Fig. 1: Trial Vaginal Tablet

OBSERVATIONS AND RESULTS

Demographic data, effect of treatment on various subjective and objective parameters and hemoglobin status are as follows:

Mizaj:

The maximum number of patients i.e. 37 (74.0%) were of *Balghami Mizaj* where as 10 (20.0%) cases were *Damvi* 3 (6.0%) cases were *Safravi* and no patients were observed of *Saudavi mizaj*.

Inference:

The *balghami mizaj* were prone to candida vaginitis. As the *mizaj* of female is *barid* as compared to men, the basal metabolic rate of female is low and because of the fact that *balgham* itself provide the media for the growth of micro-organisms (22).

Age:

The highest number of patients 29 (58.0%) was found in age group of 26-35 years.

Inference:

This revealed that the disease is prevalent in reproductive age group. This finding in accordance with the finding of Unani Scholars (10, 11, 19, 35).

Socio-Economic Status:

It was observed that maximum patients 38 (76.0%) belonged low income group and 12 (24.0%) to middle income group and no patients were observed in higher income group.

Inference:

Low socio-economic status, negligence are the predisposing factors for *Sailan-ur-Rehm* (1).

Occupations:

It was observed that maximum number of patients were house wives i.e. 39 (78.0%).

Inference:

They were lead a sedentary life which causes accumulation of *fuzulat* in the body result in less *istefragh* leads to *Sailan-ur-Rehm* (22).

Educational Status:

Majority of patients i.e. 27 (54.0%) were illiterate.

Inference:

Illiteracy is one of the predisposing factor for *Sailan-ur-Rehm*.

Parity:

It was observed that majority of patients 42% were of para-2-such description are also available in unani literature that *Sailan-ur-Rehm* is common in paraous women (13, 19).

Diet:

It was observed that 6 (12.0%) cases were non-vegetarian, while 15 (30.0%) cases were vegetarian and maximum no of patients i.e. 29 (58.0%) belonged to those who using mixed diet. Most of the patients who attended the study consumed mixed diet.

Inference:

Badi, saqeel, balgham producing and non-vegetarian diet are the aggravating factor for *Sailan-ur-Rehm* (26).

Contraceptive measures:

15 (30.0%) patients were not using any contraceptive measure, 13 (26.0%) had tubal ligation done, 9 (18.0%) were on OCPs, while 7 (14.0%) were using condoms, 6 (12.0%) had inserted Cu.T as contraceptive measure.

Inference:

High dose OCPs are the predisposing factor for candida vaginitis (36).

Menstrual History:

Maximum cases i.e. 42 (84.0%) were having regular cycles.

Inference:

No specific sign and symptoms were reported at the time of menstrual cycle.

Effect of the trial drug on Subjective Parameters

The effects of the trail drug are shown in Table-1.

Table-1: Effect of the trial drug on Subjective Parameters

Symptoms	Before Treatment		After Treatment			
	No. of Cases	% age	No. of Cases improved	% age	No. of cases not improved	% age
Vaginal discharge	50	100.0	42	84.0	8	16.0
Itching vulvae	50	100.0	41	82.0	9	18.0
Abnormal	05	10.0	03	60.0	2	40.0

vaginal						
Burning micturition	23	46.0	17	74.0	6	26.0
Dysuria	12	24.0	09	75.0	3	25.0
Dyspareunia	09	18.0	06	66.6	03	33.3
Low backache	34	68.0	22	64.7	12	35.3
Pain in lower abdomen	26	52.0	21	81.8	05	19.2

White discharge per vaginum:

All the 50 patients had the complaints of white discharge before starting the treatment and at the end of the study 42 (84.0%) cases showed improvement due to qabis habis, mujaffif properties of the trial drugs (09, 28,34,40,41,42). Showed a p value <0.001 as highly significant.

Itching Vulvae:

Itching vulvae was also present in all 50 patients at the baseline visit and at the end of study 41 (82.0%) cases were improved due to Anti-septic, anti-fungal, and purifying action of drugs (04,09,28,34,46). It Showed a p value < 0.001 as highly significant.

Abnormal vaginal odour:

The abnormal odour were noticed in 5 (10.0%) and 3 cases were improved at the end of study due to dafetaffun action of the trial drugs (04,29,30,34).

Burning micturition:

Burning micturition were present in 23 cases (46.0%) at the baseline visit at the end of study 17 cases (73.9%) were improved due to *mudir-e-bol* property of the trial drugs (16,24,29,31,34).

Dysuria:

12 (24.0%) patients out of 50 complaints of dysuria and after treatment 9 (75.0%) patients showed improvement.

Dyspareunia:

Nine patients c/o dyspareunia, at the end of the study six cases were improved.

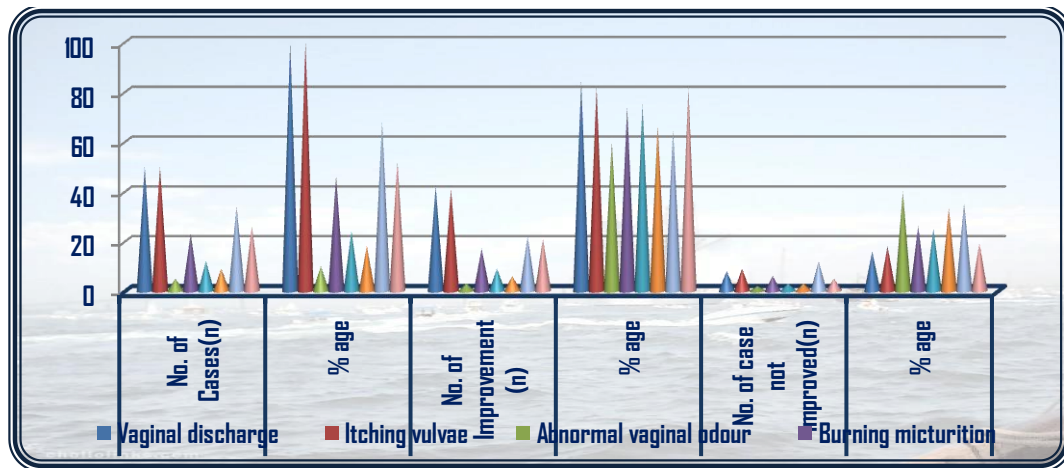
Low Backache:

34 patients complained of low backache at the baseline visit and at the end of treatment 22 (64.7%) cases were improved and 12 (35.3%) had no relief due to the anti-inflammatory action of the trial drugs.

Pain in Lower Abdomen:

It was observed that 26 cases out of 50 had c/o pain in lower abdomen before the treatment, 21 (81.8%) cases were improved after treatment. The symptoms were significantly relieved after treatment due to the effect of the test drugs (16,17,18,24,29).

The Effect of The trial drugs on symptoms (Subjective Parameter) are shown in Graph 1.



Graph- 1: Effect of the Trial Drugs on Symptoms (Subjective Parameter).

PAP smear was done in 30 cases out of 50 before and after treatment. Before treatment the smear eosinophilic, non-branching, non-septate hyphae and box car arrangement of pseudohyphae, violet coloured pear shaped spores were seen lying free and attached to the hyphae. There is extensive neutrophilic infiltration after treatment the smears were normal and negative for fungal element.

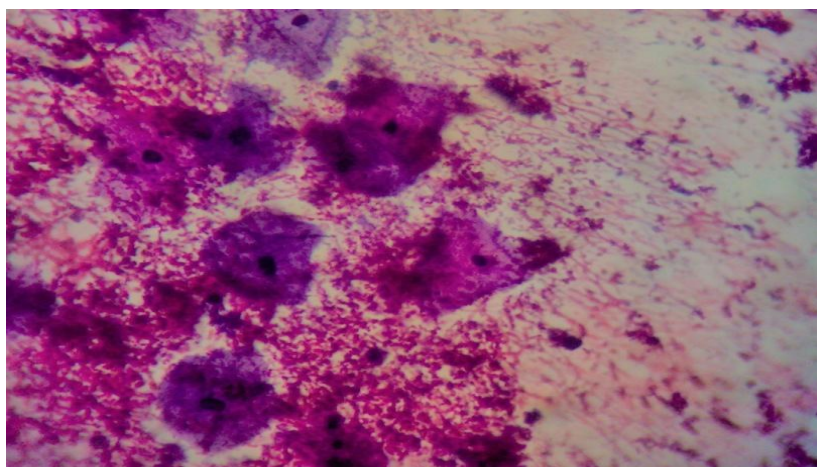


Fig. 2: Cervical smear shows polyhedral intermediate cells with vesicular oval nuclei and bluish cytoplasm and superficial cells with eosinophilic cytoplasm. Thick bundles of candida hyphae are seen enmeshing small dot like spores and neutrophils H & E 40.

Fungal culture was done in 5 cases out of 50. Before treatment - the culture showed germinating spore and hyphae which was found to be pathogenic in subsequent sub-cultures and after treatment the fungal growth was not observed.

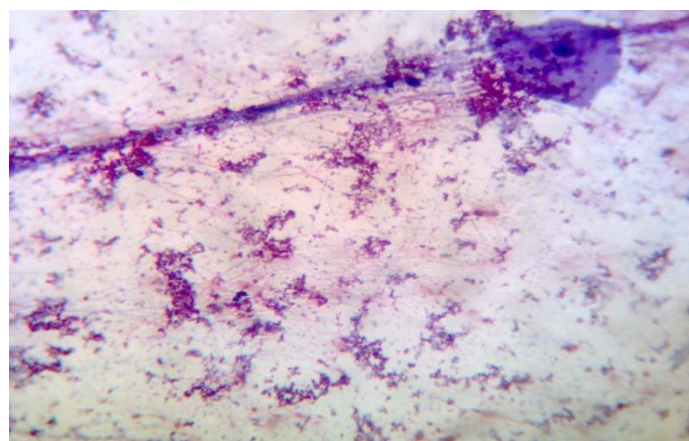


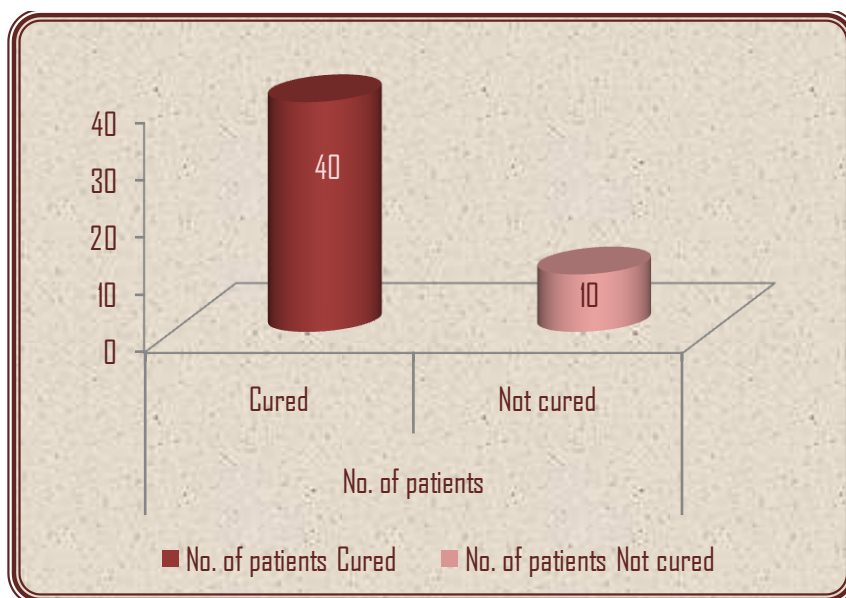
Fig. 3: Smear from culture of candida. The violet colored Budding yeast like spores show germinating eosinophilic Hyphae sprouting from the spores.MGG*40.

Hb %:

The mean Hb% was 9.1 ± 1.1 before beginning the study which was 9.2 ± 1.1 at the end of study. On applying paired 't' test on difference of Hb% i.e. 0.15 ± 0.75 it was found that $t = 1.3$ and $p > 0.5$. Hence, the effect of the trial drug on Hb% was insignificant.

Effect of the trial drug on Objective Parameters :

This specific component for curve revealed that trial drugs were more effective in eliminating mycelia tangles and spores of candida. The ($p < 0.001$) after completion of treatment and it was found to be highly significant which are shown in Graph 2.



Graph -2: Effect of the Trial drug on Objective parameter

The Effect of the trial drug on objective parameters are shown in Table 2.

Table 2: Effect of the trial drug on objective parameters.

Candida Vaginitis	No. of patients		P value
	Cured	Not Cured	
KOH	40	10	< 0.001

Assessment of response of treatment

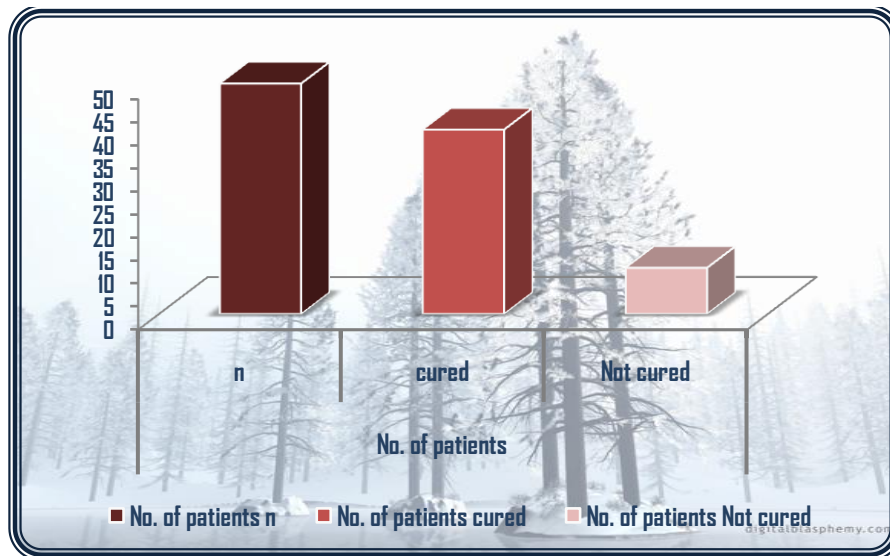
There are two ways to assist the response of treatment, which are as follows:

Therapeutic Outcomes:

In this study trial drug showed rate of 80% (40 out of 50) which is statistically highly significant. ($P < 0.001$). The effects of therapeutic outcomes are shown in Table 3 and Graph 3.

Table – 3: Therapeutic Outcomes

	No. of Patients			P. Value
	n	Cured	Not cured	
Candida Vaginitis	50	40	10	< 0.001



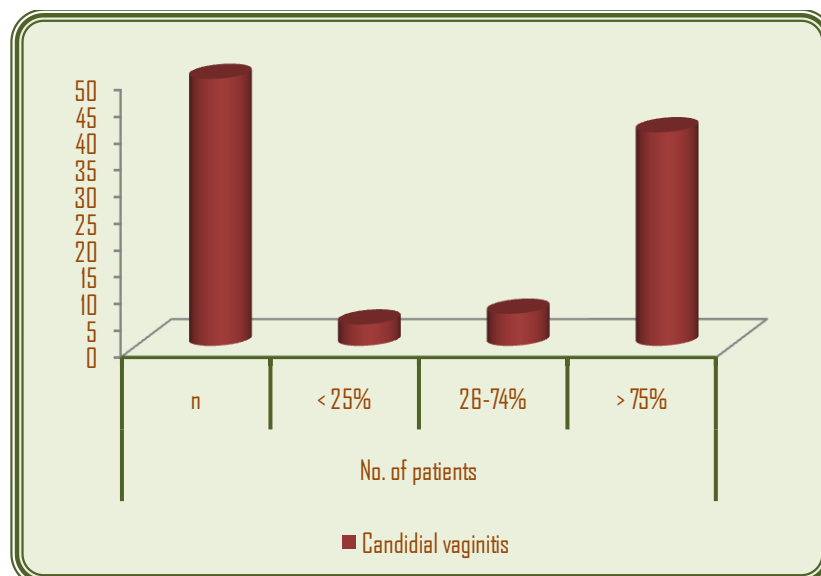
Graph 3: Therapeutic Outcomes

Symptomatic Relief:

Majority of patients i.e. 40 out of 50 had more than or equal to 75% relief in all symptoms. 6 patients had moderate relief and only 4 patients had minimal relief with p value < 0.001 statistically highly significant the effect of Symptomatic relief are shown in Table 4 and Graph 4.

Table- 4: Symptomatic Relief :

Group	No. of Patients				P. Value
	N	< 25%	26 – 74%	> 75%	
Candida Vaginitis	50	04	06	40	< 0.001



Graph 4: Symptomatic relief

CONCLUSION

In this prospective study, patients of *Iltehab-e-Mahbal* (Candidal vaginitis) were selected as per inclusion criteria. A vaginal tablet (prepared by four drugs namely Suhaga, Satwar, Baboona and Dar-e-Hald all in equal quantity) of 1 gm was kept in vagina overnight for consecutive 14 nights and Aab-e-Murawwaqain was given orally 25 ml twice a day for 14 days. The patients were followed up at each cycle after menstruation for 3 consecutive cycles.

The trial revealed that this disease is common in the patients of Balghami mizaj in reproductive age. After treatment, it was found to be statistically highly significant ($p < 0.001$). It reveals that Unani drugs are effective treatment in candidial vaginitis. This may be attributed to its mizaj, Anti-inflammatory, Anti-Bacterial, Antifungal, Antiseptic properties. No untoward side effects were noticed during the treatment.

On the basis of above observation it may be recommended that trial Unani formulation is a safe and effective treatment for *Iltehab-e-Mahbal* (especially Candidial Vaginitis).

FOR FUTURE RECOMMENDATION:

Phase III clinical trial can be carried out to further assess the efficacy and safety of unani formulation on large number of patients.

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