



ORIGINAL RESEARCH PAPER

Pharmacology

EVALUATION OF PRESCRIBING PATTERN OF ANTIFUNGAL DRUGS IN DIABETIC PATIENTS AT SAGAR HOSPITAL, BENGALURU

KEY WORDS: diabetic mellitus
fungal infections T.corposis

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Introduction

Dermatology is the branch of medicine dealing with the skin, nails, hair and its diseases. It is an immense subject, embracing some 2000 conditions, yet paradoxically, some 70% of the dermatology work in the UK is caused by nine types of skin disorders such as skin cancer, acne, atopic eczema, psoriasis, viral warts, other infective skin disorders, benign tumor and vascular lesions, leg ulcers, contact dermatitis and other eczemas¹. It is important to recognize that the fungi are not related to bacteria (Monera). To define the exact limits of the groups in a few words is virtually impossible, however generally speaking fungi are eukaryotic, heterotrophic, unicellular to filamentous, rigid cell walled, spore bearing organisms that usually reproduce by both sexual and asexual means. Further they are insensitive to antibacterial and antibiotics. Like plants, fungi have rigid cell wall and are therefore non-motile, a feature which separates them from animals².

The cutaneous mycoses are superficial fungal infections of the skin, hair or nails. Essentially no living tissue is invaded, however a variety of pathological changes occur in the host because of the presence of the infectious agent and/or its metabolic products.

The principle aetiological agents are dermatophytic moulds belonging to the genera *Microsporum*, *Trichophyton* and *Epidermophyton* which cause ringworm or tinea of the scalp, glabrous skin and nails; *Malassezia furfur*, a lipophilic yeast responsible for pityriasis versicolor, follicular pityriasis, seborrhoeic dermatitis and dandruff; and *Candida albicans* and related species, causing candidiasis of skin, mucous membranes and nails⁵.

DERMATOPHYTOSIS (Tinea or Ringworm):

- Etiological agents are called dermatophytes- "skin plants". Three important anamorphic genera, (i.e., *Microsporum*, *Trichophyton*, and *Epidermophyton*), are involved in ringworm.
- Dermatophytes are keratinophilic- "keratin loving". Keratin is a major protein found in horns, hooves, nails and skin.
- Ringworm- disease called "herpes" by the Greeks, and by the Romans "Tinea" (which means small insect larvae).

Clinical manifestations of ringworm infections are called by different names on the basis of location of infection sites:

Tinea capitis -

Ringworm infection of the head, scalp, eyebrows, eyelashes

Tinea favosa -

Ringworm infection of the scalp (crusty hair)

Tinea corporis -

Ringworm infection of the body (smooth skin)

Tinea cruris -

Ringworm infection of the groin and buttock (jock itch)

Tinea unguium/Onychomycosis -

Ringworm infection of the nails

Tinea barbae -

Ringworm infection of the beard

Tinea manuum -

Ringworm infection of the hand

Tinea pedis -

Ringworm infection of the foot (athlete's foot)

Tinea versicolor -

Skin discoloration, fungal infection that causes white to light brown patches on the skin.

YEAST/CANDIDIA

Candidiasis is a primary or secondary mycotic infection caused by members of the genus *Candida*. The clinical manifestations may be acute, sub acute or chronic to episodic. Involvement may be localized to the mouth, throat, skin, scalp, vagina, fingers, nails, bronchi, lungs, or the gastrointestinal tract, or become systemic as in septicemia, endocarditis and meningitis.

In healthy individuals, a *Candida* infection are usually due to impaired epithelial barrier functions and occurs in all age groups, but are most common in the newborn and the elderly.

They usually remain superficial and respond readily to treatment. Systemic candidiasis is usually seen in patients with cell-mediated immune deficiency, and those receiving aggressive cancer treatment, immune-suppression or transplantation therapy.

Several species of *Candida* may be the aetiological agents, but most commonly are, *Candida albicans* and rarely *C. tropicalis*, *C. krusei*, *C. parapsilosis*, *C. guilliermondii*, *C. kefyr* (*C. pseudotropicalis*) and *C. (Torulopsis) glabrata*. All are ubiquitous and occur naturally on humans, especially *C. albicans* which is recognized as a commensal of the gastrointestinal tract^{8,9}.

Clinical manifestation of candidiasis infections are called by different names on basis of location of infection sites: Oral candidiasis, Cutaneous candidiasis, Genital candidiasis, Systemic candidiasis⁵



Fig No.1: Candidiasis infection based on their location⁶.

PATHOGENESIS:

Fungi are recognized by the cells of their innate immune system (eg: dendritic cells and macropages) which bind components of fungal cell walls using pattern recognition receptors (PRRs) on their surface. C-type lectin receptors (CLRs, eg:dectin – 1) are particularly important PRRs in antifungal unity, although several other PRRs are also involved including their **Toll-like** (TLRs, eg. TLR2). When PRRs bind fungi, they signal using their intracellular tail or associated molecules (FcRy) resulting in phagocytosis, initiation of killing mechanisms (e.g.: production of reactive oxygen species) and also help the development of adoptive immunity. Adoptive immunity to fungi is only partially understood, although it seems that CD4+T cells that make IFNy(Th1) or IL-17(Th17) provide the best protection during fungal infections, as this helps to drive effective killing by innate effector cells such as neutrophils and macrophages⁷.




Fig No.2: Images of KOH test¹

KOH Preparations

- A slide.
- Scrap border of the lesion.
- Add 1-2 drops of KOH 20% and heat gently
- Examine at 40x
- Look for hypha

Fungal Culture test:

- DTM (Dermatophyte Test Medium): Yellow to red is (+).
- Sabouraud's agar Media.

b.HeterocyclicBenzofurans	Dermatophytosis	Interacts with polymerized microtubules, disrupt the mitotic spindle thus inhibits the fungal mitosis	Headache, Rashes, Peripheral neuritis, Gieffects, confusion, Vertigo, Blurred vision.
c. Echinocandins	Candidiasis Aspergillosis	Inhibits the synthesis of glucans in fungal cell wall	Flushing,Nausea ,Fever, Phlebitis at site of infection
Antimetabolites	Cryptococcosis Candidiasis Chromoblastomycosis	Interferes with fungal DNA synthesis by inhibiting thymidylate synthase enzyme	Anemia, Neutropenia, Thrombocytopenia, Alopecia, Skin rashes, Itching, Diarrhea, Vomiting, Hepatitis.
Azoles	Dermatophytosis Candidiasis Bastomycosis Histoplasmosis Coccidioidomycosis Aspergillosis Sporotrichosis	Impair ergosterol synthesis by inhibiting 14α-demethyase	Local irritation, Rashes, Itching, Gynaecomastia, Oligospermia, Anorexia, Amenorrhoea, Nausea, Loss of libido, Vomiting Hepatotoxicity Hypokalemia.
Allyamine	Dermatophytosis Candidiasis	Inhibits 2,3 epoxides and blocks ergosterol synthesis	Nausea, Diarrhea, Rashes, Itching, Dyspnea,.

TREATMENT⁸

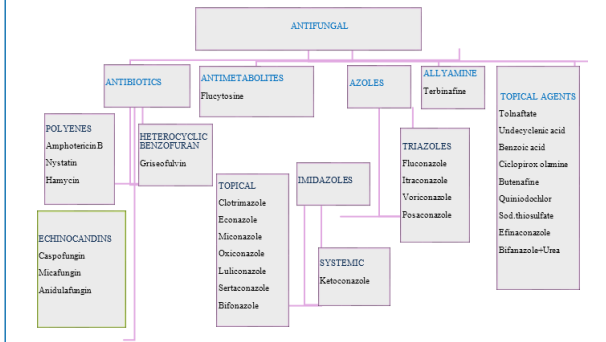


Figure No.3: Antifungal treatment chart⁸

Table No.1: Action of antifungal drugs and their useful spectrum of activity⁸

Drug class	Spectrum of activity	Mechanism of Action	ADR
Antibiotics a.Polyenes	Aspergillosis Blastomycosis Candidiasis Cryptococcosis Coccidioidomycosis Histoplasmosis Mucormycosis Sporotrichosis	Bind tightly to ergosterol in fungal cell membrane, form pores and channels in the membrane and increases membrane permeability and cause death of fungi (fungicidal)	Fever,Chills,Dysponia Anemia,Nephrotoxicity,Na usea, Bitter taste,

DIABETES MELLITUS:

Diabetes is a major health problem in India. According to diabetes atlas published by the IDF it was estimated that there were 40 million diabetes in India in 2007 and this number is predicted to rise almost 70 million people by 2025⁹.According to WHO estimation that diabetes will be the 7th leading cause of death by 2030¹⁰.

The term diabetes is the shortened version of the full name *diabetes mellitus*. Diabetes mellitus is derived from Greek word **diabetes** meaning **siphon-** means to pass through in Latin word **mellitus** meaning honey or sweet. This is because in diabetes excess sugar is found in blood as well as the urine. It was known in the 17th century as the “pissing evil”¹¹.

Diabetes mellitus is a chronic disease characterized by high blood glucose levels due to absolute or relative deficiency of circulating insulin level. Diabetes mellitus could also mean a group of metabolic diseases characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both. The disease is an major degenerative ailment in the world today, affecting at least 15 million people and having complications which include hypertension, atherosclerosis and microcirculatory disorders (retinopathy nephropathy and neuropathy)¹. Diabetes mellitus is becoming a serious threat to mankind health in all parts of the world. The control and treatment of diabetes and its complications mainly depend on the chemical or biochemical agents, but the fact is that it has never been reported that someone had recovered totally from diabetes¹².

SIGNS AND SYMPTOMS^{13,14}

Type 1 DM:

- Polyuria
- Polydipsia
- Polyphagia
- Weight loss
- Diabetic ketoacidosis

Type 2 DM:

Often asymptomatic
Lethargy
Polyuria
Polydipsia
Nocturia
Less common significant weight loss
Hyperosmolar non-ketotic hyperglycemia

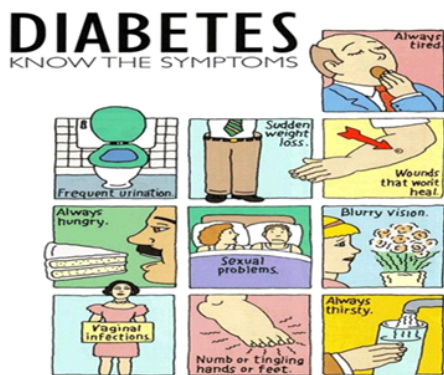


Figure No.4: Diabetes Symptoms¹⁴
RISK FACTORS^{13,14}

The risk factors for type 1 diabetes are:

- Family member with type 1 diabetes slightly increase the risk of developing the disease.
- Environmental factors
- Exposure to some viral infections

Risk factors for type 2 diabetes are:

- Family history of diabetes, Overweight, Unhealthy diet, Physical inactivity, Increasing age, High blood pressure, Ethnicity, Impaired glucose tolerance, History of gestational diabetes, Poor nutrition during pregnancy

Etiologic classification of diabetes mellitus¹⁵

1. Type 1 diabetes

- Immune mediated
- Idiopathic

2. Type 2 diabetes

3. Other specific types:

Genetic defects of β -cell function

- Chromosome 20q, HNF-4 α (MODY1)
- Chromosome 7p, glucokinase (MODY2)
- Chromosome 12q, HNF-1 β (MODY3)

Genetic defects in insulin action

- Type A insulin resistance
- Leprechaunism
- Rabson-Mendenhall syndrome
- Others

Diseases of the exocrine pancreas

- Pancreatitis
- Trauma/pancreatectomy
- Neoplasia
- Others

Endocrinopathies

- Acromegaly
- Cushing syndrome
- Glucagonoma
- Others

Drugs or chemical induced

- Vacor
- Nicotinic acid

- Glucocorticoids
- Others

Infections

- Congenital rubella
- Cytomegalovirus
- Others

Uncommon form of immune mediated diabetes

- Stiff-man syndrome
- Anti-insulin receptor antibodies
- Others

Other genetic syndrome sometimes associated with diabetes

- Down syndrome
- Klinefelter syndrome
- Turner syndrome

4. Gestational diabetes mellitus (GDM)

1. Type 1 diabetes mellitus:

This is the form of diabetes results from autoimmune destruction of β -cells of pancreas. It comprises of about 10 % cases of DM. It was previously termed as juvenile onset diabetes (JOD) due to its occurrence in younger age, it is also called as insulin dependent diabetes mellitus (IDDM) because it was known that these patients have absolute requirement for insulin replace as the treatment. This is further divided in two types¹⁶.

- Immune-mediated DM:** It is characterized by autoimmune destruction of β -cells which usually leads to insulin deficiency.
- Idiopathic DM:** Characterized by insulin deficiency with tendency to develop ketosis but these patients are negative for autoimmune markers.

2. Type 2 Diabetes mellitus:

This type comprises about 80% cases of DM. Previously it was called as maturity onset diabetes or non insulin dependent diabetes mellitus (NIDDM) of obese or non obese type. Although type 2 DM predominantly affects older individuals, it is now known that it is also occur in obese adolescent children. And many type 2 diabetes patient also require insulin therapy to control hyperglycemia or to prevent ketosis and thus they are not truly non - insulin dependent contrary to its former nomenclature.

3. Other specific etiologic types of DM:

About 10 % of diabetic cases have known etiology defect. One important subtype in this group is maturity onset diabetes of the young (MODY) which has autosomal dominant inheritance, early onset of hyperglycemia and impaired insulin secretion.

4. Gestational diabetes mellitus:

About 4 % pregnant women develop DM due to metabolic changes during pregnancy. Although they revert back to normal glycaemia after delivery, these women are prone to develop DM later in their life.

Pathogenesis of Dm¹⁶

Pathogenesis of Type 1 DM: The basic phenomenon in type 1 DM is destruction of β -cell mass, usually leading to absolute insulin deficiency.

Genetic susceptibility:

Type 1 DM involves inheritance of multiple genes to confer susceptibility to the disorder.

- It has been observed in identical twins that if one twin has type 1 immune mediated DM, there is about 50% chance of the second twin developing it, but not all.
- About half the cases with genetic predisposition to immune mediated DM have the susceptibility gene located in the HLA (human leucocyte antigen) region of chromosome 6 [MHC (major histo-compatibility complex) class 2 region], particularly HLA DR3, HLA DR4, and HLA DQ locus.

Autoimmune factor:

Studies on human models on immune mediated DM have shown several immunological abnormalities:

1. Presence of islet cell antibodies against GAD (glutamic acid decarboxylase), insulin etc.
2. Occurrence of lymphocytic infiltrate in and round the pancreatic islets termed insulinitis. It chiefly consists of CD8+T lymphocytes with variable number of CD8+T lymphocytes and macrophages.
3. Selective destruction of b-cell while other islet type (glucagon producing -cells, somatostatin producing delta cells, or polypeptide forming PP cells) remain unaffected. This is mediated by T-cell mediated cytotoxicity or by apoptosis.
4. Association of immune mediated DM with other autoimmune diseases in about 10-20 % cases such as Graves disease, Addison's disease, Hashimoto's thyroiditis, pernicious anemia.
5. Remission of immune mediated DM in response to immunosuppressive therapy such as administration of cyclosporine A.

Environmental factors:

1. Certain viral infections preceding the onset of disease eg. Mumps, measles, coxsackie B virus, cytomegalovirus and infectious mononucleosis.
2. Experimental induction with certain chemicals has been possible e.g. Alloxan, streptozotocin and petamidine.
3. Geographic and seasonal variations.
4. Possible relationship of early exposure to bovine milk proteins.

Pathogenesis of Type 2 DM:

The basic metabolic defect in **type 2 DM** is either a delayed insulin secretion relative to glucose loaded (impaired insulin secretion), or the peripheral tissue are unable to respond to insulin (insulin resistance). It is a heterogeneous disorder with a more complex etiology and is far more common than type1.

- a. Genetic factor:** Genetic components have a strong basis for type-2 rather than type-1DM. No definite and consistent gene have been identified, multi-factorial inheritance is the most important factor in development of type-2 DM.
 1. There is about 80% chance of developing diabetes in the other identical twin of one twin has the disease.
 2. A person with one parent having type-2 DM is at an increased risk of getting diabetes, but if both parents have type-2 DM the risk in the offspring rises to 40%.
- b. Constitutional factor:** Certain environmental factors such as obesity, hypertension, and level of physical activity play contributory role and modulate the phenotyping of the disease.
- c. Insulin resistance:** One of the most prominent metabolic features of type -2 DM is the lack of responsiveness of peripheral tissue to insulin, especially of the skeletal muscle and liver. Obesity in particular is strongly associated with insulin resistance and hence type-2 DM.

TREATMENT FOR DIABETES MELLITUS^{17,18}

Treatment of DM involves changes in lifestyle and pharmacological intervention with insulin or oral hypoglycemic drugs. In type 1 DM, the primary focus is to replace insulin secretion. For most patient with type 2 DM, change in life style are the cornerstone of treatment, particularly in the early stage of disease. Pharmacological intervention is secondary treatment.

Non-pharmacological treatment:

- a.** Dietary control is the mainstay of treatment of type 2 DM and plays a integral part in the management of type 1 DM.
- b.** For patients with type 1 DM, balance diet is required to achieve and maintain a healthy body weight. A meal plan consisting of moderate carbohydrate and low saturated fat should be given to patients. Eat high fiber containing foods including fruits and vegetables.
- c.** Cut down on sugar, sugary foods and use less salt.
- d.** Drink moderate alcohol.

- e.** In addition, patients with type 2 DM require caloric restriction to promote weight loss.
- f.** Aerobic exercise.
- g.** Smoking cessation.

Pharmacological treatment:

Drugs for Type-1 diabetes mellitus:

Insulin remains the mainstay of therapy for the treatment of type-1 diabetes.

Insulin treatment: Insulin is destroyed in gastrointestinal tract, and must be given parenteral usually by subcutaneous route, but intravenously or occasionally intramuscularly in emergencies. Intra-peritoneal is used diabetic patients with end stage renal failure treated by ambulatory peritoneal dialysis. Insulin lispro is an analogue, to provide constant basal insulin supply, mimic physiological post absorptive basal insulin secretion.

Drugs for Type-2 diabetes mellitus:

Table No.2: Action of anti-diabetic drugs used in NIDDM

Drug class	Available drugs	Mode of action	ADR'S
Sulphonylureas and Repaglinide	Chlorpropamide Tolbutamide Glibenclamide Glibornuride Gliclazide Glipizide Acetohexamide Tolazamide	Increase insulin secretion	Hypoglycemia GI disturbances Weight gain Allergic reactions Teratogenicity.
Biguanides	Metformin	Counter Insulin Resistance	Metallic taste, anorexia Nausea, diarrhea, skin rash Loss of weight, Hypoglycemia.
α – Glucosidase	Acarbose	Slow carbohydrate digestion	Flatulence, fullness diarrhea.
Thiazolidinediones	Rosiglitazone Pioglitazone	Selectively increase insulin sensitivity	Nausea, vomiting, anemia Weight gain oedema, heart failure, hepatotoxicity
Insulin	Insulin lispro Insulin aspart Insulin glargine Detemir Insulin	Decrease hepatic glucose production and increase peripheral glucose utilization	Hypoglycemia, blurred vision, confusion, anxiety Tremor, sweating Palpitation.

METHODOLOGY

Methodology is a systematic and coordinated way to solve research problems. Research methodology involves the systematic procedures by the researchers, which starts from initial identification of problem to its final conclusion. The study was conducted to evaluate the prescribing pattern of antifungal drugs and associated complications in diabetic patients in dermatology department, Sagar Hospital, Bengaluru. The project deals with description of methodology under the following headings: Research design, Study site, Study criteria, Source of data, Study period and Data collection and Data analysis plan.

RESEARCH DESIGN:

Hospital based Prospective and Observational study

SAMPLE SIZE:

85 patients were diagnosed with diabetic and fungal infections

STUDY SITE:

The study was conducted at Sagar Hospital, Bengaluru, a 415 bedded tertiary care multi- specialty hospital, Bengaluru. The hospital provides primary and specialized health care facilities to people in and around Bengaluru, including departments like Cardiology, Neurology, Pediatrics, Dermatology, Gastroenterology, Obstetrics and Gynecology etc.

STUDY CRITERIA:

Inclusion Criteria:

- Age ≥ 18 (Adult) and ≥ 65 (Geriatrics) patients.
- All the OPD patients with DM undergoing antifungal treatment.
- Patients suffering from superficial fungal infections.

Exclusion Criteria:

- IP patients/Pregnant women/breast feeding mothers

STUDY PERIOD:

The study was conducted for 6 months.

SOURCES OF DATA:

Patients with Diabetic and Fungal infections attending Outpatients Dermatology Department, Sagar Hospital, Bengaluru.

- Case reports of the patient.
- Laboratory details like FBS, PPBS, KOH test.
- Well designed data collection form was designed to document all the relevant demographic details
- Observation of treatment pattern.

ETHICAL COMMITTEE APPROVAL:

Institutional Human Ethical Committee clearance was obtained from College of Pharmaceutical sciences, Dayananda Sagar University Bengaluru to carry out the present study bearing the DSCP/HECD/089/2017.

METHOD OF DATA COLLECTION AND DATA ANALYSIS PLAN:

After obtaining approval and clearance from Institutional Ethics Committee (ICE), a hospital based prospective comparative study was conducted for 6 months on outpatients Dermatology Department of Sagar Hospital, Bangalore. The patients who have satisfied the study criteria were included in this study by obtaining informed consent. Demographic data was collected from the eligible patient's case sheet which includes age, gender, family history, past medical history and medication.

Relevant laboratory investigations were taken in study subject chosen as who were suffering from Diabetic and Fungal infection. From the subject the Diabetic and antifungal questionnaire score were collected and KOH test was done.

RESULTS

Table No. 3: The distribution of past medical history among study subject

DURATION OF DM	MALE	FEMALE	TOTAL
≤5	17(20%)	13(15.29%)	30(35.29%)
6-10	20(23.53%)	17(20%)	37(43.53%)
≥10	8(9.41%)	10(11.76%)	18(21.17%)
TOTAL	45(52.94%)	40(47.06%)	85(100%)

Fig No.5: The distribution of past medical history among study subject

Table No. 4: The distribution of fbs (mg/dl) among study subjects

FBS(MG/DL)	MALE	FEMALE	TOTAL
≤110	7(8.24%)	3(3.53%)	10(11.77%)
≥110	40(47.06%)	35(41.18%)	75(88.24%)
Total	47(55.29%)	38(44.71%)	85(100%)

Fig No.6: The distribution of fbs (mg/dl) among study subjects

Table No. 5: Distribution of ppbs (mg/dl) among study subjects

PPBS(MG/DL)	MALE	FEMALE	TOTAL
≤160	4(4.88%)	5(5.88%)	9(10.76%)
≥160	14(16.47%)	35(41.18%)	76(89.45%)
Total	45(52.94%)	40(47.06%)	85(100%)

Fig No.7: Distribution of ppbs (mg/dl) among study subjects

Table No. 6: List of Anti-diabetic drugs in study subjects

LIST OF ANTIDIABETIC DRUGS	FREQUENCY
GLIMEPIRIDE	21(24.71%)
METFORMIN	14(16.47%)
GLIMEPIRIDE+ METFORMIN	21(24.71%)
VOGLIBOSE	3(3.53%)
INSULIN	4(4.71%)
SITAGLIPTIN	1(1.18%)
REPAGLINIDE	3(3.53%)
PIOGLITAZONE	2(2.4%)
TENELIGLIPTIN	2(2.4%)
PREGABALIN	2(2.4%)
MECOBALAMINE	2(2.4%)
GLYCOMET	2(2.4%)
GLIPIZIDE	8(9.41%)
TOTAL	85(100%)

Fig No.8: List of Antidiabetic drugs in study subjects

Table No.7: The list of antifungal drugs in study subjects

LIST OF ANTIFUNGAL DRUGS	FREQUENCY
ITRACONAZOLE	50(58.82%)
KETOCONAZOLE	63(74.12%)
SERTACONAZOLE	29(34.12%)
LULICONAZOLE	29(34.12%)

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FLUCONAZOLE	8(9.14%)
CLOTTRIMAZOLE	13(15.29%)
OXICONAZOLE	8(9.41%)
MICONAZOLE	7(8.24%)
AMPHOTERICIN B	8(9.41%)
GRISEOFULVIN	7(8.24%)
TERBINAFINE	3(3.53%)
CICLOPIROX	9(11.59%)
AMOROLFINE	20(23.53%)
BENZOIC ACID	5(5.88%)
BIFANZOLE+UREA	4(4.71%)

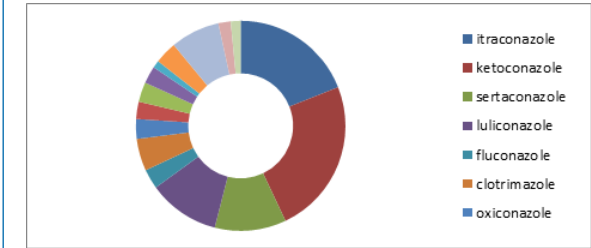


Fig No.9: The list of antifungal drugs in study subjects

Table No.8: The list of fungal infection in study subjects

DISEASE	FREQUENCY
T.CORPOSIS	32(37.65%)
T.CRUSIS	17(20%)
T.FACIEI	6(7.06%)
T.PEDIS	11(12.94%)
T.CORPOSIS+T.CRUSIS	3(3.53%)
T.CORPOSIS+T.FACIEI	1(1.18%)
T.CORPOSIS+T.PEDIS	1(1.18%)
T.PEDIS+T.FACIEI	1(1.18%)
T.CRUMS	2(2.4%)
T.VESICOLOR	2(2.4%)
T.INCOGNITO	1(1.18%)
T.BARBAE	3(3.53%)
RINGWORM INFECTION	1(1.18%)
ONCHOMYCOSIS	4(4.71%)
TOTAL	85(100%)

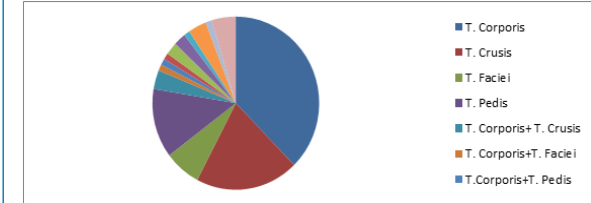


Fig No.10: The list of fungal infection in study subjects

Table No.9: The prognosis status of fungal infection after treating with antifungal drug among diabetic patients

PROGNOSIS	FREQUENCY
CURED	37(43.53%)
MODERATELY CURED	44(51.76%)
RECURRENCE	4(4.71%)
TOTAL	85(100%)

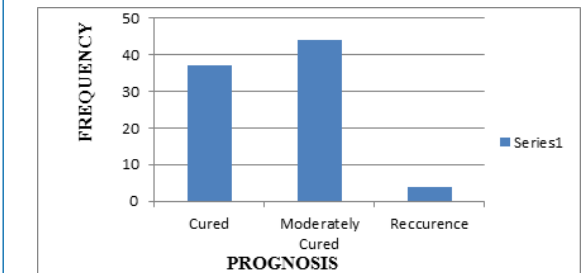


Fig No.11: The prognosis status of fungal infection after treating with antifungal drug among diabetic patients

DISCUSSION

The cutaneous mycoses are the superficial fungal infections of the skin, hair or nails. Essentially no living tissue is invaded, however a variety of pathological changes occur in the host because of the presence of the infectious agent and/or its metabolic products. The principle aetiological agents are dermatophytic moulds belonging to the genera *Microsporium*, *Trichophyton* and *Epidermophyton* which cause ringworm or tinea of the scalp, glabrous skin and nails; *Malasseziafufur*, a lipophilic yeast responsible for pityriasis versicolor, follicular pityriasis, seborrhoeic dermatitis and dandruff; and *Candida albicans* and related species, causing candidiasis of skin, mucous membranes and nails.

Commonly used antifungals Antibiotics: griseofulvin, amphotericin B, nystatin, etc; Azole: cotrimazole, miconazole, ketoconazole, itraconazole, etc; Antimetabolites: flucytosine; Allylamine: Terbinafine; Topical agents: Tolnaftate, Ciclopirox, Bifanzole+Urea, etc.

Diabetes mellitus is a chronic disease characterized by high blood glucose levels due to absolute or relative deficiency of circulating insulin level. Diabetes mellitus could also mean a group of metabolic diseases characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both. The control and treatment of diabetes and its complications mainly depends on the chemical or biochemical agents, but the fact is that it has never been reported that someone had recovered totally from diabetes.

Treatment of DM involves changes in lifestyle and pharmacological intervention with insulin or oral hypoglycemic drugs. In type 1 DM, the primary focus is to replace insulin secretion. For most of the patients with type 2 DM, change in life style is the cornerstone of treatment, particularly in the early stage of disease. Pharmacological intervention is a secondary treatment.

Diabetes mellitus is associated with a higher incidence of certain infections, including fungal infections like rhinocerebralzygomycosis (RCZ) and cutaneous candidacies. As the path physiology of increased susceptibility to infection the treatment of infectious diseases in diabetic patients is very complex, a general therapeutic approach does not exist yet. Appropriate diabetes control remains as the best preventive measure. But however, the effective drug therapy is very often required. Fluconazole has proven efficacy in prophylaxis, treatment and suppressive therapy of both systemic and superficial fungal infections, especially in candidacies and cryptococcosis. Therefore it is used routinely against fungal infections in diabetics (FID)

A total of 85 patients diabetic with fungal infections were enrolled in the study. The mean age of subject candidates was 44.38±14.57, median was 43.5.

The minimum and maximum ages in candidates were 18 years and 80 years respectively.

Among the total of 85 patients, 40 were female and 45 were males as illustrated in Table no. 3, male patients are majority.

FROM DIABETES AND ANTIFUNGAL QUESTIONNAIRES:

1. Duration of past medical history among study subject:
Table no. 3 shows among 85 subjects under the study. They were divided according to their past medical history of DM. Out of 85 study subjects 17(20%) male and 13(15.29%) female were having DM for 5 years or less. 20(23.53%) males and 17(20%) females were having DM since 6-10 years. 8(9.42%) males and 10(11.76%) females were having DM for more than 10 years.

2. Distribution of FBS (mg/dl) among study subjects:
The mean FBS level of study subjects was 147.83±37.04, median was 144. The minimum FBS level found in patient was 100mg/dl and maximum FBS level was 296mg/dl.

Table no. 4 shows FBS (mg/dl) levels of the subjects under the study. Among that the patients having FBS level less than

110mg/dl were 7(8.24%) males and 3(3.53%) female in total 10(11.77%) study subjects. The patients having FBS level more than 110 mg/dl were 40(47.06%) males and 35(41.18%) females. 3. Distribution of PPBS (mg/dl) among study subjects: The mean PPBS level of study subjects was 218.11±55.06, median was 196.5. The minimum PPBS level found in patient was 133mg/dl and maximum PPBS level was 359mg/dl.

Table no. 5 shows PPBS (mg/dl) levels of 85 study subjects. Among 85 subjects under the study 4(4.88%) males and 5(5.88%) females' subjects were having PPBS levels 160mg/dl or less than that and 14(16.47%) male and 35(41.18%) female were having PPBS levels more than 160mg/dl.

4. List of antidiabetic drugs in study subjects:

Table no. 6 shows the list and frequency of antifungal drugs used by the subjects under the study. The most frequently used antidiabetic drugs were glimeperide and combination of glimeperide with metformin in 21(24.71%) patients each, metformin in 14(16.47%) patients, glipizide in 8(9.41%) patients, insulin in 4(4.71%) patients, voglibose and repaglinide in 3(3.53%) patients each; pioglitazone, teneligliptine, pregabalin, mecobalamine, glycomet were given to 2(2.4%) patients each and sitagliptin was given to 1(1.18%) patient.

5. List of antifungal drugs in study subjects:

Table no. 7 indicates the list of antifungal drugs prescribed to the subjects under the study. The most frequently used antifungal drugs used in patients was ketoconazole in 63(74.12%) patients, itraconazole in 50(58.82%) patients, sertaconazole and luliconazole was prescribed to 29(34.12%) patients each, amorolfine was prescribed to 20(23.53%) patients, clotrimazole given to 13(15.29%) patients, cicloprox given to 9(11.59%) patients, oxiconazole and amphotericin B were prescribed to 8(9.41%) patients each, miconazole and griseofulvin were prescribed to 7(8.24%) patients each, terbinafine in 3(3.53%) patients, bifazole urea to 4(4.71%) patients and benzoic acid was prescribed to 5(5.88%) patients.

6. List of fungal infections in study subjects:

Table no. 8 indicates the list of fungal infections seen in 85 subjects under the study. The most common fungal infection observed was *T. corporis* in 32(37.65%) patients, *T. cruris* in 17(20%) patients, *T. pedis* in 11(12.94%) patients, *T. faciei* in 6(7.06%) patients, *T. corporis* with *T. cruris* was seen in 3(3.53%) patients, *T. barbae* was seen in 3(3.53%) patients, *Onchomycosis* was seen in 4(4.71%) patients, *T. cruris* and *T. vesicolor* was observed in 2(2.4%) patients each, *T. incognito* and *Ringworm infection*, *T. corporis* with *T. faciei* was seen in 1(1.18%) patient, *T. corporis* with *T. pedis* was seen in 1(1.18%) patient each, *T. pedis* with *T. faciei* was seen in 1(1.18%) patient.

7. The prognosis status of fungal infection after treating with antifungal drug among diabetic patients:

Table no. 9 shows the follow up of the prognosis status of fungal infection after treating with antifungal drugs among diabetic patients. Among 85 patients 44(51.76%) patients were moderately cured, 37(43.53%) patients were cured and 4(4.71%) patients were under recurrence

CONCLUSION:

The present study reveals that fungal infection is common in diabetic patients when compared to normal individual and the treatment for fungal in diabetic patients will seems to be difficult. Among 85 patients under study the most common fungal infection observed was *T. corporis* in 32 patients, *T. cruris* in 17 patients, *T. pedis* in 11 patients, *T. faciei* in 6 patients, *T. corporis* and *T. cruris* was seen in 3 patients and the remaining fungal infections vary from 1-3%. Among 85 patients 44 patients were moderately cured, 37 patients were cured and 4 patients were under recurrence. The most frequently used antifungal drug was ketoconazole in 63 patients, itraconazole in 50 patients, sertaconazole and luliconazole to 29 patients, amorolfine to 20 patients, clotrimazole was given to 13 patients, cicloprox given to 9 patients, oxiconazole and amphotericin B were prescribed to 8

patients, miconazole and griseofulvin to 7 patients, terbinafine to 3 patients, bifazole urea to 4 patients and benzoic acid to 5 patients. In conclusion the most common fungal infection was with *T. corporis* and the most commonly used antifungal drug was ketoconazole and cure rate was moderate.

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