TURKISH REPUBLIC OF NORTHERN CYPRUS
NEAR EAST UNIVERSITY
HEALTH SCIENCE INSTITUTE

CANDIDA ALBICANS INFECTION IN PREGNANT AND NON-PREGNANT WOMEN

KAZHAL SYAMAND ISMAEL GARDI

MASTER OF SCIENCE THESIS

MEDICAL MICROBILOGY AND CLINICAL MICROBILOGY
DEPARTMENT

ADVISOR

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“ **APPROVAL**

The Directorate of Health Sciences Institute

This study has been accepted by the Thesis Committee in Medical Microbiology and Clinical Microbiology Programme as Master Thesis.

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According to the relevant articles of the Near East University Postgraduate Study – Education and Examination Regulations, this thesis has been approved by the above mentioned members of the thesis committee and the decision of the Board of Directors of the institute.

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Director of the Institute of Health Sciences

Near East University

DECLARATION

Hereby, I declare that this thesis study is my own study, I had no unethical behaviors in all stages from planning of the thesis until writing there for, I obtained all the information in this thesis in academic and ethical rules, I provided reference to all of the information and comments which could not be obtained by this thesis study and took these references into the reference list; and, had no behavior of breeching patent rights and copyright infringement during the study and writing of this thesis

Kazhal Syamand Ismael GARDI

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ABSTRACT

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Vulvovaginal candidiasis VVC remains one of the most common infections of the female genital tract. It has been estimated up to 75% of women will have at least one episode of vaginal candidiasis during their lives. The aim of study was to determine the frequency of Candida species isolation from pregnant and Non-pregnant women and study significance between two groups. Methods: The prevalence of study was perform among females *Candida albicans* infection in Erbil-Iraq city/Rizgary Hospital. The samples was collect in gynecology department in Rizgary Hospital that harbor history with vaginal infection in both pregnant and non-pregnant women. In addition, the collection of information's was according to the special questioners that related to the current study. Results: The study design arrange according to two group (Pregnant 50 % and Non pregnant women 50%), pregnant women have *Candida albicans* infection was 13%, Non Candida was 24%, also13% was Candida spp infection. Moreover, in Non-pregnant women there was 26% have *Candida albicans*, 6% was Non Candida, and 18% was infected with Candida spp. And our statistical analysis P. values was less than (P 0.05), therefore there was greeters infection was associated with Non pregnant women than pregnant group amongst in *Candida albicans* and Candida spp, moreover, according to Non Candida infection are mostly found in pregnant women than Non pregnant women. Conclusion: We concluded the vaginal infection in pregnant women have *Candida albicans* disease less in count when comparing to the Non pregnant women group that have greatest number of positive with *Candida albicans* infection.

***Keywords*:** Vaginal Swab, Culture, pregnancy& Non-Pregnant, *Candida albicans*

ÖZET

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Vulvovajinal kandidiyaz VVC, kadın genital sisteminin en yaygın enfeksiyonlarından biri olmaya devam etmektedir. Kadınların% 75'inin yaşamları boyunca en az bir vajinal kandidiyaz atağı geçireceği tahmin edilmektedir. Çalışmanın amacı, gebe ve gebe olmayan kadınlardan Candida türlerinin izolasyon sıklığını belirlemek ve iki grup arasındaki çalışmanın önemini araştırmaktı. Yöntemler: Çalışmanın yaygınlığı Erbil-Irak / Rizgary Hastanesi kadın C.albicans enfeksiyonu arasında yapıldı. Numuneler hem hamile hem de hamile olmayan kadınlarda vajinal enfeksiyon öyküsü barındıran Rizgary Hastanesi jinekoloji bölümünde toplandı. Ayrıca, bilgi toplanması mevcut çalışma ile ilgili özel soru soranlara göre yapılmıştır. Bulgular: Çalışma tasarımı iki gruba (Pregnat% 50 ve Hamile olmayan kadınlar% 50) göre düzenlenmiştir, gebe kadınlarda C.albicance enfeksiyonu% 13, Candida dışı% 24, ayrıca% 13 Candida spp enfeksiyonu olmuştur. Ayrıca, gebe olmayan kadınlarda% 26 oranında C.albicance,% 6 oranında Candida olmayan ve% 18 oranında Candida spp. İstatistiksel analizimiz P. değerlerimiz daha düşüktü (P 0.05), C.albicance ve Candida spp'de gebe olmayan kadınlarla hamile gruptan daha fazla selamlayan enfeksiyon vardı, ayrıca Candida dışı enfeksiyona göre daha çok Hamile olmayan kadınlardan daha hamile kadınlar. Sonuç: Gebe kadınlarda vajinal enfeksiyonun C.albicance hastalığına göre sayıca daha az olduğu sonucuna varıldı.

Anahtar Kelimeler: Vajinal Sürüntü, Kültür, gebelik ve Gebe Olmayan, *Candida albicans*

TABLE OF CONTENTS

LIST OF TABLES

LIST OF TABLES

LIST OF ABBREVIATIONS

VVC	**Vulvovaginal Candidiasis**
GPI	**Glycosylphosphatidylinositol**
RVVC	**Recover Vulvovaginal Candidiasis**
ALS	**Agglutinin-Like Sequence**
PCR	**Polymer Chain Reaction**
KOH	**Potassium Hydroxide**
SDA	**Sabouraud Dextrose Agar**
SPSS	**Statistical Package Social Sciences**

SECTION ONE: INTRODUCTION

1.1. Scope of the study

The prevalence study will perform among females *Candida albicans* infection in Erbil-Iraq city in Rizgary Hospital. The samples will be collect from patients who visit gynecology department in Rizgary Hospital that have history with vaginal infection from pregnant and non-pregnant women, in order to comparing candidiasis between to group, In addition, the collecting information's according to the special questionnaires that related to the current study.

Isolation and determination of *Candida albicans* vaginal infection will perform by, (i) Direct wet microscope method of determination characteristic of fungi by microscopical examination, (ii) Golden standard method (Culture) the Sabouraud Dextrose Agar use for growth of fungi, (iii) Gram stain for detect regular of constriction

Aim of the study was focus in:

1. Incidence of *Candida albicans* in among pregnant and non-pregnant women
2. Isolation and Determine the role of *Candida albicans* in vulvovaginaitis
3. Evaluation *Candida albicans* among pregnant & Non-Pregnant women

To investigate the latest prevalence and risk of multiple *Candida albicans* infection in women who suffer from vulvovaginalis, as well as evaluation the risk among pregnant and non-pregnant women.

2. GENERAL INFORMATION

2.1. Taxonomy

Candida albicans and other species can cause *Candidiasis;* which is a fungal infection that can affect people. Whether it is a minor condition such as oral or genital thrush, or it's a fatal systemic infection; mostly patients who are already seriously diseased with some other illness will be affected. Infections with *Candida albicans* have become an interesting case, because fatal conditions became much more common and new disorders associated with Candida has been known. Needless to say, the Candida yeast infections also have scientific value as we could use them as a model to help us understand of the pathogenesis of Candidiasis, and the biochemical nature of the yeast as well. It was midway of 19th century when oral candidiasis's clinical nature was explained and the causative agent was recognized. 166 synonyms are being used for members of the genus *Candida albicans* worldwide. Not to mention that Candida genus itself is embraced in Deuteromycetes class and because they have no known sexual stage or significant phenotypic characteristic, hence they are known as a "taxonomic pit". The members are heterogeneous and yeasts with basidiomycetous and ascomycetous are included. 150 to 200 species are now acknowledged in the genus. An example is imperfect asporogenous yeasts which are characteristically white and are capable of pseudohyphae formation. Characterization of species in the genus are done primarily via colony morphology, moreover; the ability to ferment, and to utilize carbon. Seven members of the genus have great clinical significance, and especially *Candida albicans* which is very aggressive in men. Candida tropical is, parapsilosis, stellatoidea, lusitaniae, glabrata, and krusei also cause Candida infections. DNA of Candida stellatoidea and *Candida albicans* is somewhat highly homologous, this is why stellatoidea is considered a form of albicans. Studies show that sucrose negative *Candida albicans* are of two distinct types: (i) Candida stellatoidea I. (ii) Candida stellatoidea II.

Further analysis show that type I can't be distinguished from *Candida albicans*, whereas type II is an alternative or mutative form of *Candida albicans*. And *Candida albicans* species are believed to be obligatory associated with warm-blooded animals and it is thought to be a dimorphic fungus. Reviews also show an interesting fact about this imperfect yeast which is a diploid not capable to undergo sexual cycle or meiosis, forming a haplophase fungus (Z Laczkowski, K., et al, 2015; Soll, D. R., 2003; Negroni, R., et al, 2020: Naglik, J. R., et al, 2019).

2.2. Candida albicans

Candida albicans is an opportunistic pathogen and a leading cause of death due to fungus in the immunocompromised population. It causes acute infections by colonizing the skin and mucus surfaces. More than eighty percent of women will suffer from vaginal candidiasis at least once in their lifetime. Severe infections of bloodstream usually occur and will be life threatening if it was not diagnosed in the right time, as it could cause the development of resistant strains in healthcare centers around the globe in the future. In addition, the yeast is a pathogen which is polymorphic, undergoing transitions including: (i) Budding. (ii) Pseudohyphal growth forms. (iii) Hyphal growth forms. The pathogen's capability to switch between these different forms is associated with the virulence of the fungus. As the mutative forms which can't undergo hyphal growth are less aggressive in models used such as a mice models, than are the more aggressive, wild forms. Understanding the principles of switching between the different morphologies matter, as it helps us understand the pathogenic behavior of the fungus. *Candida albicans's cell wall is the site in which pathogen to host interactions occur, it is also the targeted site for vaccines and antifungals.* The cell wall is made up of chitin, a layer of sugar and proteins. The proteins are mostly bound to polysaccharide glucans through GPI. The genetic material of *the fungus* consists of a hundred and fifteen proteins-GPI that can be fastened to the wall of the polypeptides, but will only be presented in special cases. There are only about twenty to thirty wall proteins being shown at one time.

These proteins have multiple functions including:

- Acquisition of iron for tissue invasion
- Adhesion
- Protection against the immune response

If we take a look at hyphal growth, we would see that when the surface of the cell is expanded, it is limited to a small and specific region at the peak of the hypha. And during this whole process of growth, the zone is active, and the fungus produces cells which will extend apically starting from the tiny area. In the primary step of budding however and only here, the bud achieves a critical expanse, the growth is turned off, and global expanding occurs. It is also important to note that localizing the yeast or hyphal cell's cytoskeleton mirrors the variations which happen in their morphogenesis. In every hyphal cell, polarization of the cytoskeleton to the tip of the hypha is seen. In yeast cell forms however, patches of the cortical actin in only small budded cells are noticed in the apical expansion area. It is thought that the cytoskeleton is necessary for apically polarized growth, as a drug called chloropropham which works on actin filaments is seen to terminate hyphal growth. Polarization mechanism of the cytoskeleton to the hyphal crests is not known, in part due to obligatory diploid behavior of our yeast without a sexual cycle, and this is also a reason which made it difficult to study the organism. Hyphal cells are of great significance and value when it comes to biofilm formation and also taking over host tissues. On the other hand, dispersal in host tissues is done by the yeast cells. This switch or transition could also cause the liberation of enzymes which cause degradation and proteins are formed that help against oxidative stress. In the yeast and hyphal cells, locked non virulent mutative forms are seen and for reaching full, its necessary to transit efficiently from a stage to another. The opportunistic fungal pathogen *Candida albicans* is a leading cause of fungal death in a clinical setting in the immunocompetent populace and *is consider one of* skin colonizes and mucosal surfaces which lead to acute infections over 80% of all women experience at least one bout of vaginal candidiasis in their lifetime, life threatening bloodstream

infections occur regularly and are often fatal if not diagnosed in time which may in future cause the emergence of antifungal resistant strains in hospitals around the world the need for better treatment options and new antifungals and vaccines **(**Luo G**.**, et al, 2010; Klis F. M**.**, et al, 2010; Monteoliva L**.**, et al, 2011**).**

There are various scientific reports of the recently described about the yeast species *Candida dubliniensis* designate to be worldwide manifestation and it is recognized this fungus is phylogenetically narrowly interconnected to other fungi which termed as *C. albicans*, Moreover the *C. dubliniensis* has been principally improved from the preferable area which is oral cavity of human immunodeficiency virus (AIDS) infected patients and is infrequently existent in cases of candidemia. Confirmation for the inducibility of a stable to antifungal (fluconazole) resistance in vitro in *C. dubliniensis* strains may designate a developing pathogen for immunocompromised patients getting long term fluconazole prophylaxis, however, the pathogenic potential of *C. dubliniensis* leftovers unidentified. Moreover and it is since the *C. dubliniensis* is usually originate in mixed culture with *C. albicans* the color of their colonies during primary culture on CHROMagar Candida, a medium particularly recommended for uncovering mixed yeast cultures, has been investigated. Dark green colonies were found to be indicative of *C. dubliniensis*, in contrast to light green colonies, which indicate the presence *C. albicans*, however, this phenomenon has been found to be nonreproducible after subculture and storage of isolates (Peltroche-Llacsahuanga, H., et al, 2000).

2.3. VulvoVaginal Candidiasis

Any condition which causes abnormal discharge from the vagina, or abnormal scent, redness, itching, burning sensation and irritation, is termed as vaginitis. Causes of vaginitis could be due to bacteria (bacterial vaginosis) forty to fifty percent of the cases, fungus (vulvovaginal candidiasis) twenty to twenty-five percent of the cases, or parasite (trichomoniasis) fifteen to twenty percent of the cases. Vaginitis could also be due to causes which are noninfectious which are not that common and account for

about five to 10 percent of the cases, and they include atrophic vaginitis, inflammatory vaginitis as well as irritant vaginitis. In order to diagnose vaginitis, we symptoms and clinical examination comes handy. Moreover, laboratory tests also aid in our diagnosis. For diagnosing vaginosis caused by bacteria, Gram Stain is the standard key, however amsel criteria could also be used. Recent tests capable of detecting DNA *Gardnerella vaginalis* or the activity of vaginal sialidase could have same or similar effects and results of a Gram stain. Treatment of bacterial vaginosis could be done with metronidazole whether oral or intravaginal, as well as clindamycin used in intravaginal way. When it comes to diagnosing vulvovaginal candidiasis, some available tests which can aid include: examining clinical features, DNA probe, and potassium hydroxide microscopy. Complicated vulvovaginal candidiasis could be diagnosed using culture in which strains of *Candida other than albicans are identified*. Fluconazole orally or azoles topically could be used for treatment of vulvovaginal candidiasis. However, in pregnant women, only azoles shall be used topically. If a patient with trichomoniasis is symptomatic or is a woman with a high risk, it is recommended that amplification of nucleic acid be used for diagnosis. Patients having trichomoniasis will be treated via tinidazole or metronidazole orally. It is also important to know that in this case, not only the patients themselves but their sex partners shall also take treatments. Patients with noninfectious vaginitis will be treated according to the cause. For example, hormonal or non-hormonal therapy could be used for atrophic vaginitis. Steroids and clindamycin being used topically could treat inflammatory vaginitis.

VVC is an acute inflammatory illness which happens to be one of the great reasons for gynaecological visits because it might affect about seventy-five percent of middle-aged women. During physical examination we could see discharge, redness of the vulva, itchiness, and patient might feel severe pain during sexual intercourse called dyspareunia. Risk factors might be oral contraceptives, gestation, DM which is not controlled, and severe usage of antibiotics. After removing or controlling the risk factors, vulvovaginal candidiasis could be treated. For many women this disease won't be frequent, however sometimes in some women there will be bouts of the disease

about four times each year with much more severe signs and symptoms which is called RVVC. Although Fluconazole used on a long time basis could help elongate the periods in which the patient is asymptomatic, but it won't result in curing the disease. New studies about transmission of the disease tell us that the commonness of RVVC is higher than it was expected to be before which is about seven to eight percent of women who undergo the first bout of symptoms, in other words one to two percent of all women will be affected yearly all over the world. RVVC decreases the ability of young women in their work and their social life and their quality of life as a whole as it causes severe and intense discomfort and symptoms. Moreover, condition of the affected women will be further worsened as these patients seek to feel better and hence follow advertisements and products which are not prescribed by doctors. If we ask what factor causes a women having VVC to transit or not transit to RVVC, then we still do not have the answer. Even though we can say that a small amount of the cases in which there is transition to RVVC could be because of the persistence and lasting underlying cause VVC, but in most of the cases the cause is unknown as it can happen in when there's not any risk factors known. This could mean that there is a genetic cause as it is noticed in chronic muco-cutaneous candidiasis. The increased ratio of RVVC could be due to a combination of genetic factors in which a group of genes are being problematic in individuals as well as environmental factors. Polymorphisms are being recognized in RVVC patients which include: SNP, IL 4 & 22, not regulated T cells and many more. So, we can say that recent evidences tell us that gene polymorphisms could put women in risk (Borges, S., et al, 2014; Puel, A., et al, 2012; De Luca A, et al, 2013).

2.4. Virulence factors

In order to describe any organism's success in colonizing and invading host tissues, we can describe their virulence factors in example TM. These might include what is related to their adhesion, their cell wall, and their proteolytic enzymes. For the organism to be successful as a pathogen it needs to produce its cell wall, because it is

needed for growing and protecting them from osmotic stress and it is where there will be contact of the organism and the environment. The receptors and ligands however motivate the organism to colonize onto the host's tissues and cells. On the other hand, proteolytic enzymes help penetrating tissues. The cell wall of the organism which acts as a virulence factor is made up of twenty-three percent of mannan, forty to sixty percent of glucan, less than one to nine percent of chitin, six to twenty-five percent of glucans proteins, one to seven percent of lipids. Studies about the cell wall recognized a complicated architecture with differences in the thickness, which is made up of many layers, as it is seen by the variability in the density of the electron of the layers and their phenotype are different as well which might be due to their stage in growth or fixation process. The components of the wall layers are identified by stains, antibodies, and lectins. It is said that mannan is present through the whole cell wall, chitin and glucan make up the inner cell wall primarily, mannan and mannnoprotein make up the outer layers of the wall, which is similar to a coat or a capsule, and it will be removed during an infection. Mannan used to be known as the main surface antigen before understanding its chemical nature. Long ago, Candida albicans was said to be of two types, A and B. But after a study on buccal cells of healthy donors, it was shown that both serotypes adhered to the cells to a much greater degree than other species, but they themselves had the same degree of adherence. Studies also show that the hydrophilic cells are much less virulent than the hydrophobic cells. Tests were done for hydrophobicity of the surface of the cells using polystyrene microsphere assay and for the capability to bind to HeLa cells. If the yeast has decreased capability for adherence in vitro, it'd as well be disable to cause infections in vivo. In contrast, if they are more active and capable in adhering to buccal cells and if they formed more active proteinase enzyme, then they'd be more lethal in mice models.

Those which adhered to buccal epithelial cells in a very strong way, had very high enzyme activity as well and were also very pathogenic. The activity of the proteinase enzyme of the yeast is related to its virulence. In infected patients, proteinase antigens and antibodies will be seen. These enzymes are made up of

carboxyl proteinases and are able to degrade Immunoglobulin A, which is the main mucous membrane Ig. Some of the enzymes have the ability to degrade keratin or collagen. After purifying the enzyme and sequencing its genes, we notice that it has two mechanisms for virulence. Producing enzymes is related to being capable to colonize onto host tissues, and proteolytic activity is related to invading tissues (Monika, S., 2019; Verma, A. H., et al, 2017; del Valle Castillo, G., et al, 2018; Sardi, J. D. C. O., et al, 2018; De Bernardis, F., et al, 2018; Canela, H. M. S., et al, 2018).

2.5. Morphology

Candida albicans has two morphological forms which are yeast or mycelilal forms and this fungus can grow into either of the forms. Even though it can be a harmless flora in mammals, but it can also cause fatal illnesses in a host who is not that healthy anyways. Candida albicans is the most common fungus causing diseases in humans in which infections occur on surfaces of the body. But the disease could also be systemic and much more severe to the extent of threatening the life of the patient. As we have mentioned before, candida albicans embraces several morphological forms including yeasts, hyphae, and pseudohyphae. Elongated yeast cells put onto chains, make up a pseudohyphae which are different from the mycelial cells or true hyphae and also in the component of the cell wall. In short, unicellular yeast is the habitual form of growth of the organism in which it will be dividing by budding. We could reproduce this form in vitro using many liquid and solid media with temperatures of forty Celsius. The fungus could also be multicellular in the form of mycelilal cells in which its proven that pathogenicity is related to changing into this form. This mode could be made up of pseudohyphal, hyphal, or both. Extension of germ tubes in yeast cells could result in true hyphae, this production of germ cells could be done in vitro using under a number of condition and using many media, but mostly high temperature of thirty-five to thirty-nine Celsius is needed. We can see pseudohyphae both in vivo and in vitro and it represents an atypical form of dividing through budding.

These elongated chains are narrowed where the budding occurs. Extending and branching of hyphae could result in the formation of a multicellular mycelium, or maybe lateral or terminal budding will restart. In special cases, cells with very large and thick walls called chlamydospores, could be produced. Even though studies of the biochemical and genetic factors which tend to hold up and control the fungus's polymorphism is not well understood, but the transition which occurs in this organism is very interesting both because of it relation with its pathogenic behavior, but also because it could be a model for understanding a lower eukaryote's morphogenesis. There is no report showing the organism being stuck as a mycelium at twenty to twenty-five Celsius (ambient temperature) (Kadosh, D., 2019; Kornitzer, D., 2019; Vellanki, S., et al, 2019).

2.6. Replication

An impressive characteristic of this yeast, is how it's capable to grow into either a yeast cell which is unicellular, psedohyphae which is elongated and filamentous, or a hypha. Pseudohyphae and hyphae are different from each other as the latter doesn't have the constrictions or the narrowing at the region of dividing and is less wide than psedohyphae. They form long filaments in the shape of a tube in which the side are entirely parallel and there is definitely no narrowing where the dividing of the septa occurs. Again and again there are many differences between psedohyphae and hyphae, both in their cycle of life and in their mechanism for growth polarization. A factor which will determine the virulence of the organism is morphological plasticity. For instance, during infections of mucosa hypha mode has a responsibility in it, as it will be invading and damaging endothelial and epithelial cells through the liberation of enzymes (hydrolytic). In order to get access to the bloodstream and cause candidaemia, we first need to do endothelial penetration. Studies done in vitro, show us that the form responsible for invasion, is the hyphal form and samples of biopsy from the sick people who had this infection of mucosa also represents the hyphal mode in the epithelium. Moreover, if macrophages try to eat the yeast form of cells, they would try to hide and

escape through transition into the hyphae. All these roles of hyphae aside, it is still not under discussion whether hyphae form is actually needed for virulence (Dalle, F., et al, 2010; Zhu, W., & Filler, S. G., 2010; Uppuluri, P., et al, 2006; Finkel, S. E., 2006; Crampin, H., et al, 2005).

2.7. Adhesins and invasins

C. albicans has a specialized set of proteins (adhesins) which mediate adherence to other *C. albicans* cells to other microorganisms, to abiotic surfaces and to host cells. Debatably for induced endocytosis, the fungus expresses specialized proteins on the cell surface (invasins) that mediate binding to host ligands (such as E-cadherin on epithelial cells and N-cadherin on endothelial cells), thereby triggering engulfment of the fungal cell into the host cell. Indeed, even killed hyphae are taken up, indicating that induced endocytosis is a passive process that does not require the activities of viable fungal cells. Two invasins have been identified so far, namely Als3 (which also functions as an adhesin, see above) and Ssa1. Ssa1 is a cell-surface expressed member of the heat shock protein 70 (Hsp70) family. Both *als3*Δ/Δ and *ssa1*Δ/Δ mutants exhibited reduced epithelial adherence and invasion, and reduced virulence in a murine model of oropharyngeal candidiasis. Als3 and Ssa1 bind to host E-cadherin and likely induce endocytosis by a clathrin-dependent mechanism; however, macropinocytosis has also been implicated in *C. albicans* induced endocytosis. In contrast, active penetration is a fungal-driven process and requires viable *C. albicans* hyphae. It is still unclear exactly which factors mediate this second route of invasion into host cells. Fungal adhesion and physical forces are believed to be crucial. Secreted aspartic proteases (Saps) have also been proposed to contribute to active penetration. Lipases and phospholipases, on the other hand, have not been shown to contribute to this process (Karthik, L., et al, 2014; Calderone, R. A., & Clancy, C. J., 2011; Dalle, F., et al, 2010; Vickers, N. J., 2017).

2.8. Biofilm formation

Another very necessary cause of the virulence of Candida albicans, is its ability of biofilm formation on both biological and non-biological surfaces. The most usual substrates for the formation of a biofilm are catheters, non-biological dentures, and biological mucosa Surfaces. Producing a biofilm will be done in sequence. First the the microorganism binds to one of the common surfaces, then the cells will proliferate forming hyphae in the superior part of the film, in addition there will be building up of materials from extracellular matrix, and the last but not least, the yeast cells will be distributed or dispersed through the biofilm. When organism are arranged and appear as a complex and mature biofilm, their resistance will be much more to antifungals or factors of the host's immune system than the planktonic fungi. This increased resistance is indeed related to the complicated content of biofilms including its architecture, matrix, higher number of pumps which will efflux drugs, and also metabolic plasticity. Distribution of the cells throughout the biofilm is associated with virulence, because in an experiment being done on infected mice models, the distributed yeast cells were more aggressive or virulent. Recently, the main Hsp 90 or Heat Shock Protein 90 is being recognized as a factor responsible for the distribution happening in a biofilm produced by the candida albicans fungi. This protein is also needed for resistance of the biofilm against antimicrobial drugs. There are many factors of transcription which take control in forming a biofilm. For instance; EFG1, TEC1, & BCR1. In a study being done recently by Nobile et al. further regulators of the biofilm which were unknown before, including ROB1, BRG1 and some other. If either of these factors are being deleted, it will result in the formation of an abnormal biofilm inside the body of an infected rat model. Ptoducing material of the extracellular matrix requires other factors such as ZAP1 transcription factor which is responsive to zinc and it downregulates glucan which is the main content of the matrix of the biofilm. For upregulating the glucan and its further production however, glucoamylases GCA 1 & 2, exoglucanase, and glucan transferases will help. Expressing glucoamylases require ZAP1 to control them but the others do not need this downregulator and they

work independent on it. If a mutative form does not have Bgl2, Xog1, or Phr1 then the biofilm which is produced will be much more fragile for an attack by the fluconazole antimicrobial both inside a living and outside of it (in vitro). Studies also show that the biofilm produced by this fungus is resistant against neutrophils and they will not cause the production of free radicals, which is thought to be because of the beta glucans that exist in their matrix ((Finkel, J. S., & Mitchell, A. P., 2011; Fanning, S., & Mitchell, A. P., 2012; Taff, H. T., et al, 2012).

2.9. Pathogenicity

One of the most common organism causing superficial invasive infection in humans is Candida species which cause candidiasis. The infection involves mucosa, such as what happens in mouth or vagina which make up about forty million cases annually. This high ratio of colonization of the organism could be related to diseases of the gut such as ulcerative colitis and crohn's disease, and if we decrease this load of pathogen the severity of the illness will also be decreased. In addition, in immunocompromised patients, the risk of infection will keep on increasing. Like most of the other fatal systemic infections, candidiasis could also find the opportunity to infect hosts through the mucosa. That is why it is very important to understand the way epithelium recognizes the microorganism and takes actions against it. Many of the fungus species of the genus are actually a part of the human normal flora, but some could be bad guys and turn into opportunistic pathogens causing an infection in the host tissues by turning from a flora into a virulent microorganism which happens due to changes in the environment of the host. This organism rarely causes disease in healthy individuals, however they do find opportunities to proliferate when the immune system of the host becomes locally or systematically impaired, and in turn result in candidiasis. We can say that Candidiasis is of three types: 1. Cutaneous 2. Mucosal 3. Systemic. In the cutaneous type; skin and skin appendages will be involved. In the mucosal type; oropharynx, esophagus, & vulvovagina are involved. And finally systemic candidiasis means there is a bloodstream infection such as

candidemia and IC. In patients that suffer from AIDS, we could notice superficial, mucosal, & cutaneous types of the disease.

In immunocompromised adult women we'd see vaginitis, and in infants usually thrush in the oropharynx is seen. In individuals which have cancer or had a transplant, we mostly see systemic candidemia or what is calles invasive candidiasis as these patients' immunity is suppressed. Right now, this disease which is caused by this fungus is the 4th cause for hospital acquired infections at a rate of about eight to ten percent, and the ratio of the cause of death due to candidemia is fifteen to thirty-five percent and stays high related to which species is the causative agent. Candida albicans mostly causes infection of the mucosa. The rate of vaginal infection due to the fungus could be about 20 percent, but there are differences in the investigations which are done and data which are collected, as menstruation and pregnancy alters the prevelance of infection. For instance, the incidence increases during the 3rd trimester because the pH of the vagina becomes lower and more favorable for colonization. Discomfort and agony takes over women of any age during the disease and should never be taken for granted. Managing chronic oral infection is hard and patients will not be so active or functional which is why the pathogen could spread throughout the host till it reaches the viscera of the human. During cutaneous or mucocutaneous conditions, samples are taken from lesions for physical examination. When the fungus in in an environment or with a thirty-seven Celsius temperature, it will produce germ tubes, and when they are growing on specific media including detergent tween 80-containing cornmeal agar, they produce chlamydospores and hyphae as well. Recently, several kits and equipment exists for identifying the species. In the past, C.albicans was the most significant member of the group being known to be causing disease, but lately, tropicalis has also been noticed to be responsible for a number of infections in hosts which are compromised (Pfaller, MA, & Diekema DJ., 2007; Kumamoto, CA., 2011).

2.10. Diagnosis

Dysuria, itching, pain, edema, fissure, thick discharge, redness, and skin-picking suggest a clinical diagnosis. In females with known sign and symptoms of vaginal infection, diagnosis could be made in these ways:

1. A wet preparation of saline & ten percent of potassium hydroxide.
2. Microscopical examination of the vaginal discharge using gram stain to identify yeasts or hyphae or pseudohyphae.

These examinations help us in the case of itches, burns, rashes, unpleasant odors, or abnormal discharges to come to a conclusion about the suspect we had about fungal infection of vagina.

3. Cultures could also be used to identify the presence of fungus.

In vaginitis which is caused by candida we have a normal pH of more than four in the vagina. If during wet mount preparations we used ten percent of potassium hydroxide, we would be able to visualize the yeast & mycelia better, because it causes the material in their cells to be sort of destructed as they might come in our way and cause an obstruction in the fungus. Every single female having signs and symptoms of vulvovaginal candidiasis must be examined using wet mounts and potassium hydroxide. And obviously if the result is positive, treatment is needed. Those with negative results but existing symptoms however, require further examinations using culture medias. If culture was not possible, empiric therapy shall be taken into consideration. It also won't harm to know that having positive culture results but no known symptoms do not mean we are ought to treat the individual, this is because about ten to twenty percent of females already have this fungus and other yeasts as part of the normal flora of their vagina as well. Even though PCR tends to be a very accurate test for the diagnosis of many diseases, but in this case the gold standard is still culturing. Vulvovaginal candidiasis sometimes occurs with sexually transmitted disease. Most of the women who are healthy but also caught the infection, usually have no precipitating factor to be identified (Martínez, R., et al, 2020; Weissenbacher, T., et al, 2009).

2.11. Protection

Protection and preventions are always better than treatments, hence we shall take some time to talk about protections as well. Here we begin. One of the ways that we can prevent candidiasis and mainly the vaginal type, is wearing cotton underwear. And we shall wash the vagina with water daily and avoid any so-called cosmetic products which are said to give the private a better odor or appearance. Because these things tend to alter the balance of vaginal flora which is not accepted by them and will be harmful rather than being helpful. Stress, diet, and behavior also affects vaginal pH balance, and so could minimize or increase risk of infection depending how we deal with them. Sometimes following antibiotic treatment women will eat food containing bacteria which are good and also a culture media for example yogurt, so that the risk of bacterial or fungal vaginitis is decreased. It is not proven however, that taking yogurt or probiotics will reduce the risk of developing an infection. Studies used to say that the role of using probiotics for treating vaginal infections is possible if it is used with or instead of antibiotics. But recently their potency and efficacy is questioned in treating recurrence of infection. After all, there is not enough evidence to entirely accept or deny how useful probiotics can be for treating vaginal infection due to bacteria (Anukam, K., et al, 2006; Vujic, G., et al, 2013; Bradshaw, C. S., et al, 2012; Senok, A. C., et al, 2009).

2.12. Treatment

Reducing symptoms is our aim while treating the infection. Fungi are eukaryotic like humans, and so we should be very careful at what we target while using drugs as our targets are limited. In about nineteen fifties, the very first effective antifungal drugs were presented which were amphotericin B & nystatin. After the development of cancer drugs, the activity of 5-fluorocytosine against fungus was also known. Now, imidazole derivatives are considered as one of the paramount antifungals. However, most of them are not used clinically because of how they also

act on human cells. There is also azole which can be topically and oral fluconazole. The choice of treatment depends on the condition of the patients and also on their experience with the drugs. For example, in patients who are not pregnant, there is no drug better than the other when it comes to efficacy and treatment. And the ratio of cure for all of them would be about eighty percent. Data tell us that patients mostly prefer oral drugs. But there are several things that we consider when we want to choose between an oral or a topical treatment. The topical treatments have a faster onset of action and puts the patient in comfort in a shorter time OR it causes allergy and results in even further distress. Now if we count the advantages of oral fluconazole, it'd be the one dose usage of it, and the fact that it won't make a mess like suppositories or creams. As for disadvantages, they include side effects which are systemic mainly affecting the GIT, or causing toxicity and drug interactions. Another note to be considered for married couples, is the fact that topical creams contain oil and could decrease the latex in condom and result in an unexpected pregnancy. Most of the patients tend to self-diagnose and treat themselves using topical treatments which are available in pharmacies and do not need doctor prescriptions. Studies tell us that even if women have history of VVC, they can't tell if the cause of a second or third bout of vaginitis is fungal again, hence one can't self-diagnose themselves in an accurate need and consulting medical care is always necessary (Workowski, K. A., & Bolan, G. A., 2015; Workowski, K. A., 2015).

2.13. Treatment *VVC in Pregnancy*

Unfortunately, VVC is common in pregnancy. The centers for disease control and prevention advise pregnant women with VVC to only use topical azole for a period of seven days. Although there is not enough data, but it is thought that oral treatments are related to higher risk of birth defects or miscarriage, especially if used in a high dose.

Someone with complicated VVC needs more potent treatments. We shall also make sure whether there has been history of candidiasis or the previous bout was due to another cause. In individuals who had severe VVC, re-administrating fluconazole 3 days after day one of treatment has given good results and has prevented recurrence as well. In contrast, the same thing being done in recurrent VVC did not have that good result, for recurrent VVC due to the very bad guy which we shall know so well by now which is called candida albicans therapy will be done in this way: for a week or two we will start our primary treatment using three doses of 150 milligrams of fluconazole every three days. Then our weekly therapy starts with the same amount of the same drugs for six months. For most of the patients, this way of treatment soothed their pain and discomfort.

If we realize there is no significant respond to our therapy with fluconazole, we shall do culture to see whether the cause of the infection is something other than candida albicans, as the other causes don't respond to fluconazole that much. Econazole, ketoconazole, miconazole, & clotrimazole which are imidazoles which are used topically, are more useful for elimination. In some other study, it was seen that terconazole which is also used topically, tends to helps with symptoms as well and treat patients in a ratio of about fifty percent. And for those patients who have infections which are due to the other causes and thus don't respond to such treatments, treating via 600 milligrams of boric acid capsule for two weeks daily will have good results. Some non-pharmaceutical products are also presented for helping with recurrent VVC. Combining data from several studies did not prove the full efficacy of probiotics for helping the infection of VVC, but more studies are needed because the size of the previously done studies was small and there are many different probiotic products as well (Falagas, M. E., et al, 2006; Howley, M. M., et al, 2016; Mølgaard-Nielsen, D., et al, 2016).

SECTION TWO: MATERIAL AND METHOD

2.1. Material

2.1.1. Devices and Tools

Equipment's	Country
Incubator	**Germany**
Oven	**Germany**
Medical Refrigerator	**Japan**
Autoclave	**Japan**
Sensitive balance	**Japan**
Centrifuge	**Germany**
Microscope	**Japan**
Disposable Petri dishes plate	**USA**
Disposable test tube 10 ml	**USA**
Safety cabinet II	**Japan**
Slides	**USA**
Cover slip	**USA**
Inoculation loops	**USA**
Swap	**USA**
Blood agar Base	**USA**
Chrom agar	**USA**

2.2. Software Programs

In our study the Statistical Package Social Sciences (SPSS) application used in order to manipulate the each result parameters with other data. The SPSS is a widely used program for statistical analysis in social science. It is also used by many of other fields include health researchers, It can handling complex data manipulations and analyses them very easy and within minutes.

2.3. Intended outcome of thesis

The prevalence study will perform among females *Candida albicans* infection in Erbil-Iraq city in Rizgary Hospital. The samples will be collect from patients who visit gynecology department in Rizgary Hospital that have history with vaginal infection from pregnant and non-pregnant women. In addition, the collecting information's according to the special questioners that related to the current study. Isolation and determination of *Candida albicans* vaginal infection will perform by, (i) Direct wet microscope method of determination characteristic of fungi by microscopical examination, (ii) Golden standard method (Culture) the Sabouraud Dextrose Agar use for growth of fungi, (iii) Gram stain for detect regular of constriction

2.4. Sample

The study will perform among females *Candida albicans* infection in Erbil-Iraq city in Rizgary Hospital. The samples will be collect from patients who visit gynecology department in Rizgary Hospital that have history with vaginal infection from pregnant and non-pregnant women. A vaginal swab collect from 100 female patient the sample divided into two group, 50 sample collect from pregnant women, and other 50 sample collect from non-pregnant women, who suffering history relate to vaginal infection in Erbil-Iraq city Rizgary hospital department of gynecology. Also

methodology of study depend on Microbiological Golden standard culture method, for all patient direct microscopical examination (Potassium hydroxide (KOH 20%) preparation is used for the rapid detection of fungal elements in clinical specimen, as it clears the specimen making fungal elements more visible during direct microscopic examination), as a primary screening tool will perform, in addition To identify the fungal of vaginal *Candida albicans* the specimen must be cultured in order to growth fungal in Sabouraud Dextrose Agar (SDA) culture media, it is most routinely used microbiological media uses of the cream colored pasty colonies usually appear after 24-48 hours incubation at 25-37°C. The colonies have a distinctive yeast smell and the budding cells can be easily seen, following, making Gram stained preparations of sample. In Gram stained smears, Candida appears as gram positive budding yeast cells (blastoconidia) and/or pseudohyphae showing regular points of constriction.

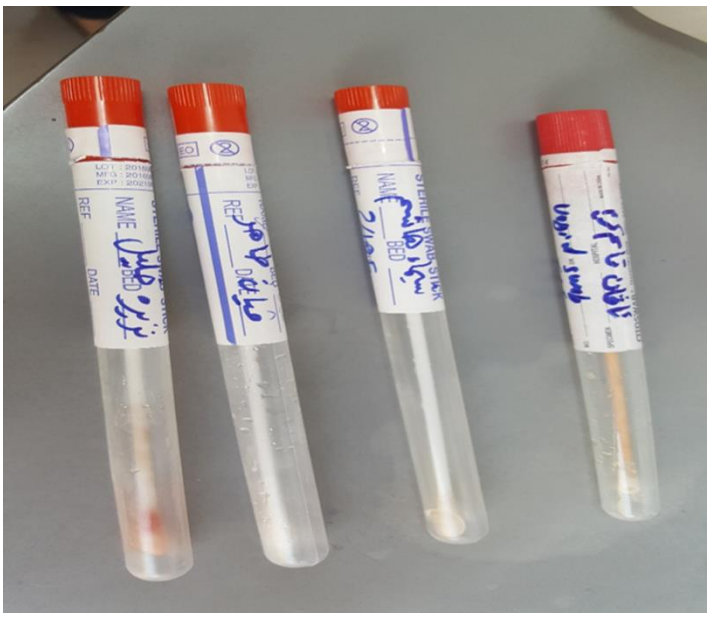

Figure 2.1: Swab of sample collection

Figure 2.2: Data collection

2.5. Media

2.5.1. Sabouraud Dextrose Agar (SDA)

I used SDA Suspend 65 g of the medium in one liter of distilled water. Heat with frequent agitation and boil for one minute to completely dissolve the medium. Autoclave at 121° C for 15 minutes. Cool to 45 to 50°C and pour into 30 petri dishes. after culturing put to incubator at 24 house in 37°C if growth the sample cream colony it is the Candida

2.5.2. Blood Agar

In blood agar make whit colony but preparation blood agar Suspend 28 g of nutrient agar powder in 1 liter of distilled water. When the agar has cooled to 45-50 °C, Add 5% (vol/vol) sterile de-fibrinated blood that has been warmed to room temperature and mix gently but well. Avoid Air bubbles. Dispense into sterile plates while liquid.

2.5.3. Chrom agar

Chromagar is a selective medium for the isolation and presumptive identification of yeast and filamentous fungi and differentiation of *candida albican*s green color, C*andida tropials* steel blu*e, Candida krusei rose* fuzzy. Suspend 45.9 grams of the medium in 1 liter of distilled water, mix will and heat with frequent agitation until complete dissolution

2.6. Germ Tube

For Identification of candida albicans used the germ tube test. Used the women serum 2ml take to tube add 1 lop in colony mixed by centrifuge after that put to

incubator at 2 o'clock in 37°C after that time inter the tube adding the drop of sample in slid covered by cover slid we see by microscopically if we see germ tube growth it is *Candida albicans* if not make germ tube we see capsule shape candida sp.

Figure2.3: Germ tube

2.7. Methods

The samples taken from patient with significant of vulvovaginal inflammation with or without swelling aching, with full questioner pattern specific to the percent study and writing the documentation. After sample collected the specimen storage according to medical laboratory advice then transferring to laboratory in order to running current processes, following, preparation two slid : (i) For all patient direct microscopically examination (Potassium hydroxide (KOH 20%) preparation is used for the rapid detection of fungal elements in clinical specimen, as it clears the specimen making fungal elements more visible during direct microscopic examination), as a primary screening tool will perform, in addition To identify the fungal of vaginal

Candida albicans (If See the budding or hyphae its fungi). (ii) Another slide will prepare to perform the gram stain there are 4 steps after make a smear on the slid from the fungi or bacteria colony then let it to dry: (i) Add the primary stain crystal violet purple dye for 1 mint to 2 mint after that washing by water. (ii) Add the Iodine mordant after for 1mint washing by water. (iii) Add the alcohol wash decolonization for 15 second after that washing by water. (v) Add safranin for 1 mint after that washing by water and take the slid to air for dry the slid after that add the drop of oil for see under the microscopically if we see the hyphae it is fungi

2.8. Statistical Data Analysis

Data analysis was performed using SPSS version 25.0 (SPSS). The present study data contain categorical were compared using perform the test associated with data suitable with Person Chi square test as appropriate. All p values were two-tailed; a p value < 0.05 was considered statistically significant.

2.9. Ethical Acceptance

RESEARCH ETHICAL COMMIITTE APPROVAL SHEET UNDER THE:

Title of the project: CANDIDA ALBICANS INFECTION IN PREGNANT AND NON-PREGNANT WOMEN in Rizgary Hospital, Erbil Iraq (Apendix A)

SECTION THREE: RESULTS

3.1. Study Population

The prevalence study will perform among females *Candida albicans* infection in Erbil-Iraq city in Rizgary Hospital. The samples will be collect from patients who visit gynecology department in Rizgary Hospital that have history with vaginal infection from pregnant and non-pregnant women. In addition, the collecting information's according to the special questioners that related to the current study. Isolation and determination of *Candida albicans* vaginal infection will performed. And the prevalence of population result was obtained as a gender all participant was female there are 50% of them was in pregnant and other 50% was Non-pregnant, the age of participant was divided between adult 97% and teen age 3%, moreover, some of the patients have history with chronic disease there are 25 % of them harbor some of chronic disease and other 75 % are normal (free from chronic disease), in addition, then full information about uses of various drug during period of time some of them used antibiotic 47 %, some other taken antifungal 1 %, other are free in uses of drug 9 %and there are some of them used both type of antibiotic with antifungal drug 43 %, and according to frequency of infection with *candida* there are 39% infected with *Candida albicans*, 30 % are non-infectious and 31 are infected with *candida spp.*

Table 3.1: prevalence of study population

Data		No.	Percent (%)
Age	**Teen**	**3**	**3.0%**
	Adult	**97**	**97.0%**
Drug	**Antibiotic**	**47**	**47.0%**
	Antifungal	**1**	**1.0%**
	Both	**9**	**9.0%**
	NO	**43**	**43.0%**
Pt. type	**Pregnant**	**50**	**50%**
	Non Pregnant	**50**	**50%**
Chronic Disease	**Yes**	**25**	**25.0%**
	No	**75**	**75.0%**
Type of infection	**Candida albicans**	**39**	**39.0%**
	Non Candida	**30**	**30.0%**
	Candida spp	**31**	**31.0%**

Table 3.2: Pregnant among chronic disease and Non chronic disease

			Chronic Disease		P.Value
			Yes	**No**	
Pregnant	**Yes**	**No.**	**11**	**39**	**0.488**
		(%)	**11.0%**	**39.0%**	
	No	**No.**	**14**	**36**	
		(%)	**14.0%**	**36.0%**	

According to the (Table 3.2) expression of significant study and according to statistical analysis observation between Pregnant state among to chronic state of disease, the prevalence result observation among two parameter was clarify as those who have pregnant and harbor chronic disease was 11.0% in addition those are free from chronic disease was 39%, Moreover, chronic disease in non-pregnant women was 14% in different to those non-pregnant and have no chronic disease was 36.0%. As a result in this experiment study show and it is noted according P.value that there is signification difference between the pregnant women and chronic disease was Non significant, and our statistical analysis P. values was more than (P 0.05).

Table 3.3: Evaluations of *Candida albicans* and drug uses

			Infection			P.Value
			Candida albicans	Non Candida	Candida spp	
Drug users	Antibiotic	**No.**	24	11	12	0.028
		(%)	24.0%	11.0%	12.0%	
	Antifungal	**No.**	0	0	1	
		(%)	0.0%	0.0%	1.0%	
	Use both of drug	**No.**	6	2	1	
		(%)	6.0%	2.0%	1.0%	
	NO drug uses	**No.**	9	17	17	
		(%)	9.0%	17.0%	17.0%	

Agreeing to the result statement and it is according to statistical analysis observation between those patients who take drug and comparing to the different result of infection state, the result show there are to some patients have been used antibiotic,

therefor the prevalence result observation among two parameter was clarify as those who taken antibiotic drug was totally 47%, there was 24% of them have *Candida albicans* infection, 11.0% doesn't have Candida infection, also there are 12% of them have different type of the Candida spp infection. Moreover there are some other patients in use of some antifungal drug, those patient used antifungal 1.0% and there was Candida spp infection isolated was 1.0% and both of *Candida albicans* and Non Candida was doesn't isolated as a infection among to taken antifungal (maybe it is drug to uses of these type of antifungal. Also there are some patient used both type of antibiotic and antifungal treatment 9.0% and there are 6 % of them have *Candida albicans* infection, Non Candida was 2%, and 1% of them have Candida spp infection. And there are some of patient didn't use any type of drug 43.0% but thy have some infection and there was 9% of them have *Candida albicans*, there was 17% have No Candida and 17% was harbor Candida spp infection. As a result in this experiment study show and it is noted according P.value that there is signification difference between the patients who take drug and infection with candida, and our statistical analysis P. values was less than (P 0.05). (Table 3.3)

Table 3.4: Candida infection among pregnant women

			Infection			
			Candida albicans	**Non Candida**	**Candida spp**	**P.value**
Pregnant	**Yes**	**No. (%)**	**13 13.0%**	**24 24.0%**	**13 13.0%**	**0.000**
	No	**No. (%)**	**26 26.0%**	**6 6.0%**	**18 18.0%**	

Conferring to the (Table 3.4) countenance of significant study and according to statistical analysis statement between Pregnant women state and it is among to the Candida infection, The study design arrange according to two group (Pregnant 50 % and Non pregnant women 50%), the prevalence result observation among two consideration was explain as those who have pregnant women that have *Candida albicans* disease was 13%, Non Candida was 24%, there was also13% associated with Candida spp infection. Moreover, the result of Non pregnant women also observed as 26% was infected with *Candida albicans* disease, 6% Associated with Non Candida infection, and there was 18% of them was infected with Candida spp. As a result in this experiment study show and it is noted according P.value that there is signification difference between the pregnant women and Non pregnant women, and our statistical analysis P. values was less than (P 0.05), therefore there was greeters infection was associated with Non pregnant women than pregnant group amongst in *Candida albicans* and Candida spp, and according to Non Candida infection are mostly found in pregnant women than Non pregnant women.

SECTION FOUR: DISCUSSION

4.1 Discussion

Candida spp. infection is one of the most common causes of vaginitis among women, and it is the most common pathogens found among women complaining of vaginal discharge in this study were *Candida albicans*, the pregnancy represents a risk factor in the occurrence of vulvovaginal candidiasis. Consequently, this study was initiated to determine the prevalence rate of vaginal colonization by Candida spp. In Erbil-Iraq city in Rizgary Hospital among to pregnant and non-pregnant women and their respective species identification by current method, and their possible correlation to the Candida species, is an important cause of wide spectrum of diseases including vulvovaginitis. The pregnant women commonly develop increased vaginal discharge which may lead to pregnancy complications like abortions, premature birth, low birth weight and other morbidities. This study aimed to determine the prevalence of Candida isolates among patients attending different Gynecological department in Rizgary Hospital, and this present study investigated the prevalence of vaginal candidiasis among pregnant women and non-pregnant women with symptoms of vaginal infection attending different gynecological clinic (Al-akeel, R. A., et al, 2013; Altayyar, I. A., et al, 2016).

In the percent study and according to the expression of significant study and the statistical analysis statement between the Pregnant women and non-pregnant women among to the Candida infection our result show the prevalence result observation among pregnant women that have *Candida albicans* was 13%, there was also13% associated with other Candida spp infection. Moreover, the result of Non pregnant women also observed was 26% with *Candida albicans* disease, and there was 18% of them was infected with Candida spp. As a result in this experiment study show and it is noted according P.value that there is signification difference between the pregnant women and Non pregnant women, and our statistical analysis P. values was less than

(P 0.05), therefore, there are greeters infection was associated with Non pregnant women than pregnant group amongst in *Candida albicans* and Candida spp. As a support to our finding also there are many of other paper agree to present finding such as in *Wise et al.* experiment and mention in his reported there are low occurrence of *Candida albicans* in pregnant women when comparing to non-pregnant women in New York (Wise, M. G., et al, 2007).

Also the is another researcher conduct in in New York by the *Trofa et al.* mention in his experimental informed that there are low occurrence of *Candida albicans* among to pregnant women when comparing to the non-pregnant women, also in agreement with our result finding which reported that the prevalence of vaginal candidiasis among pregnant women and non-pregnant were 13%, 26% respectively (Trofa, D., et al, 2008).

But there are other study demonstrates the frequent occurrence of yeasts in the vagina of pregnant and non-pregnant women in Nigeria. Asymptomatic vaginal colonization by Candida has been reported greatest in of pregnant women 40% and of non-pregnant women 20%. In the present study asymptomatic colonization of the vagina by yeasts was 13 % in pregnant women and 26% in non-pregnant women, the predominant species being *Candida albicans* (Gugnani, H. C., et al, 1989). Also the *Gugnani et al*, mention the *Candida albicans* has been described to be the predominant etiological agent of vaginal mycoses than other species of yeasts like C. parapsilosis, C. tropicalis, C. pseudotropicalis, C. krusei, C. guilliermondii (Gugnani, H. C., et al, 1989).

The *Emam et al*, results clearly demonstrated the significant differences between two groups in increase in the number of positive microscopic findings in pregnant women 48%, when compared to (26%, in non-pregnant women. The difference between the two groups is statistically significant (p= 0.022) (Emam, S. M., et al, 2012).

In contrast there are some other findings indicate as expected that Candida spp. positive culture is frequently encountered among pregnant women more as compared to those detected among non-pregnant patients, examined by direct microscopy and cultured on Sabouraud Dextrose Agar (SDA) as well as "CHROM agar Candida" medium. As expected, Candida-positive cultures were frequently observed in pregnant-test group (24%) than in non-pregnant group (17%). The frequency of culture positive was correlated to pregnancy (P=0.047) (Al-akeel, R. A., et al, 2013). Also in both of study *Altayyar et al and Holland et al*, the result showed prevalence highest value of vaginal candidiasis among pregnant women and low candida infection among to non-pregnant women Altayyar, I. A., et al, 2016 ; Holland, J., et al, 2003).

Although there is some epidemiologic evidence of increased Candida colonization and symptomatic vaginitis during pregnancy, a complete understanding of this process is lacking, and predicting vaginitis during pregnancy is unreliable in women already prone to VVC (Xu, J., & Sobel, J. D., 2004).

The high prevalence of vaginal candidiasis may due to many different reasons include; suppression of the immune system due to the pregnancy as it is among the contributing factors of vaginal candidiasis, progesterone has suppressive effect on the anti-candida activity of neutrophils while estrogen has been found to reduce the ability of vaginal epithelial cells to inhibit the growth of *Candida albicans*. Inadequate knowledge, poor personal hygiene, limited diagnostic facilities, poor dietary habits also contributed in high prevalence vaginal candidiasis (Altayyar, I. A., et al, 2016).

SECTION FIVE: CONCLUSION AND RECOMMENDATION

5.1. Conclusion

Nowadays the pregnant women usually develop to increased vaginal discharge which may lead to pregnancy complications and the vulvovaginal candidiasis are recognized as a symptomatic inflammation of the vagina which frequently involves the vulva, caused by infection with a Candida yeast. Predominant symptoms are vulvar itching and abnormal vaginal discharge (which may be minimal, a “cheese like” material, or a watery secretion).

According to the result observation and it is countenance of significant study of statistical analysis between Pregnant women and non-pregnant women among to the Candida infection we concluded that the vaginal infection prevalence result observation among two consideration was explain as those who have pregnant women that have *Candida albicans* disease was less in count when comparing to the Non pregnant women group that have greatest number of positive patients with candida albicant infection. Therefore there was graters infection was associated with Non pregnant women than pregnant group amongst in *Candida albicans* and Candida spp, and according to Non Candida infection was mostly found in pregnant women than Non pregnant women.

5.2. RECOMMENDATION

1) These findings may help in drawing strategies in preventing and controlling vulvovaginal candidiasis that may affect women and their newborns.

2) The culture of vaginal discharge should be warranted

3) Screening protocol incorporation with routine antenatal checkup for early diagnosis of candidiasis and its treatment by recommended

4) Because of the risk of VVC, Non pregnant women should not take antibiotic without consulting a doctor and laboratory diagnostic infection.

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APPENDIX

Appendix A

Hawler Medical University
College of Health Sciences

Meeting code: E 5

Ref. No: HMM 47

Date: 10/4/2020

جامعة هولير الطبية
HAWLER MEDICAL UNIVERSITY
College of Health Sciences
کۆلێژی زانستە تەندروستیەکان

RESEARCH ETHICS COMMITTEE APPROVAL SHEET

Title of the project: candida albicans infection in pregnant and non-pregnant women

Principle investigator: Kazhal Syamanad Ismael

Co-investigators: Dr. Warkaa Faraj Ahmad, Dr. Sahar Mohammed Zaki Abdullah

Head of Committee
Prof. Kafia M. Shareef

Committee Member
Dr. Fatma A. Ali

Committee Member
Dr. Rwaa A. Hwaiz

زانکۆی هەولێری پزیشکی
لیژنەی زانستی و خوێندن بالا
کۆلێژی زانستە تەندروستیەکان

Curriculum Vitae

PERSONAL INFORMATION

Kazhal Syamand Ismael GAERDI

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Whats App Messenger Kazhal GARDI

Sex **Female**| Date of birth **10 May 1981**

JOB APPLIED FOR Master Thesis

WORK EXPERIENCE

Biologist

January 2014 -Present **Rzgary teaching hospital**

100 matry, Erbil (IRAQ)

- Working at blood laboratory.
- lots of works in floors and taking care for the patients.

July 2007– August 2007 **Central Lab. working**

Jmhury hospital

60 matry, Erbil (IRAQ)

- culturing and isolation from bacteriology Lab.

June 2003– October 2003 **Bank Clerk**

- Preparing managerial order.
- Data entry.
- Printing invoices.

EDUCATION AND TRAINING

2009– 2010 Bachelor of Biology Department, Science college Salahaddin University, College of Science, Erbil (IRAQ).

2018– 2019 Training Course

Near east University, Medicine College, Lefcosa (CYPRUS)
PhD and Master students Microbiology Laboratory practical course.

2020– One day Corona Infection Control Training Course

Médecins Sans Frontières Org., Erbil (IRAQ)
The course held to control corona infections.

PERSONAL SKILLS

Mother tongue(s) Kurdish

Other language(s)

	UNDERSTANDING		SPEAKING		WRITING
	Listening	Reading	Spoken interaction	Spoken production	
English	good	good	good	good	good
Arabic	Very good	Very good	Very good	very good	Excellent

Computer skills Knowing some programme like MS word, MS excel, MS PowerPoint.

Driving licence Yes I have.