A Study of Human Papilloma Virus (HPV) Infection of the Cervix in Egyptian Females by Cytology, Histopathology, Colposcopy and HPV Genotyping

Thesis

Submitted in Partial Fulfillment for MD Degree

"Obstetrics & Gynecology"

By

Ahmed Farid El Shazly

M.B.B.Ch., M.Sc.
Assistant lecturer of Obstetrics & Gynaecology
M.U.S.T. University

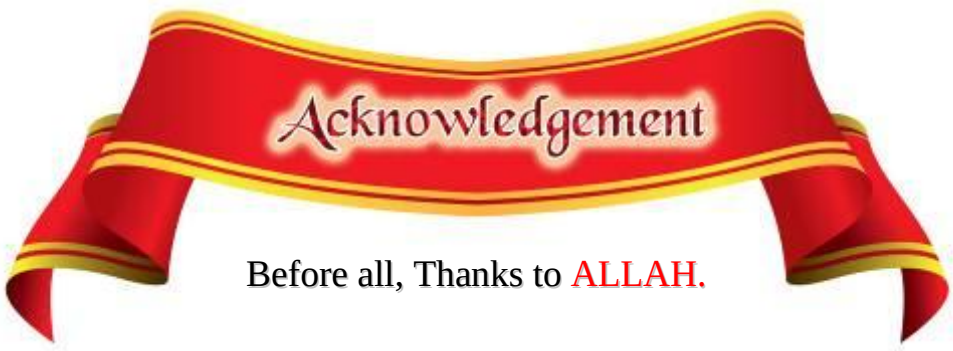
Under Supervision of

Prof. Mona Abdel Badeeh Nayel
Professor of Obstetrics & Gynaecology
Faculty of Medicine – Cairo University

Prof. Olfat Gamil Shaker
Professor of Medical Biochemistry
Faculty of Medicine – Cairo University

Prof. Hala Naguib Hosni
Professor of Pathology
Faculty of Medicine – Cairo University

Faculty of Medicine
Cairo University
2014



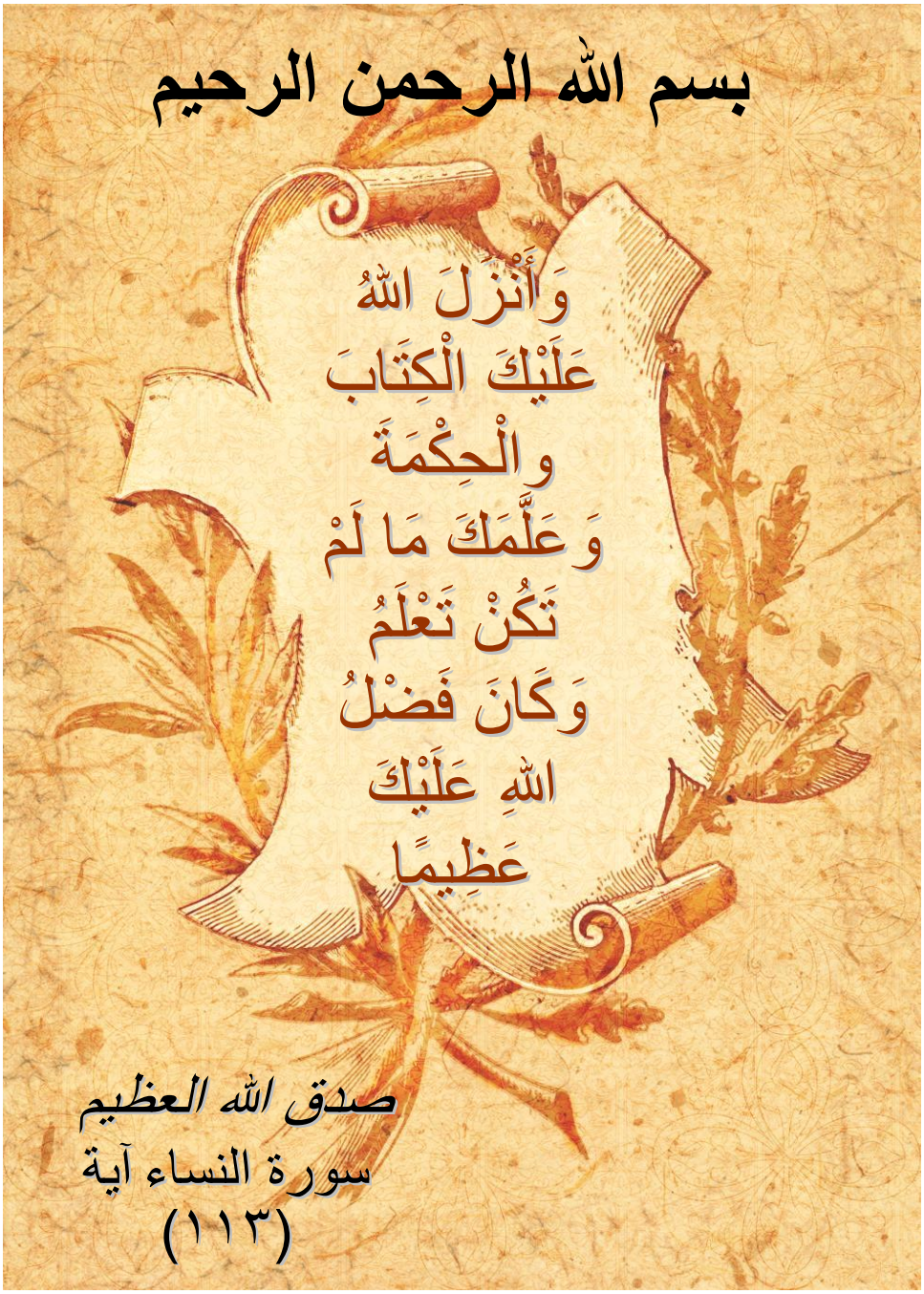
Before all, Thanks to ALLAH.

I would like to express my profound gratitude to Prof/ Mona Abdel Badeeh Nayel, Professor of Obstetrics and Gynecology, Faculty of Medicine, Cairo University for her support all through the whole work and for dedicating much of her precious time to accomplish this work.

I am also grateful to Prof/ Olfat Gamil Shaker Professor of *Medical Biochemistry*, Faculty of Medicine cairo University and Prof. Hala Naguib Hosni Professor *of Pathology Faculty of Medicine Cairo University* for their unique effort, considerable help, assistance and knowledge they offered me throughout the performance of this work.

All my thanks and gratitude to my patients for giving me their help, hoping them a good health.

Last but not the least I would like to express my deep thanks to every member in my family especially my father,my mother, my sisters, and my wife for their great support all the time and helping me from the A, B, C to the M.D.


بسم الله الرحمن الرحيم
وَأَنْزَلَ اللهُ
عَلَيْكَ الْكِتَابَ
والْحِكْمَةَ
وَعَلَّمَكَ مَا لَمْ
تَكُنْ تَعْلَمُ
وَكَانَ فَضْلُ
اللهِ عَلَيْكَ
عَظِيمًا
صدق الله العظيم
سورة النساء آية
(١١٣)

Abstract

In this study the golden standard test for detection of HPV was considered PCR-ISH tissue. We found PCR-ISH tissue was positive in 16 cases (53.33%) and 14 cases (46.6%) were negative.

The age of studied group ranged from (20-50) years with mean and standard deviation (SD) 32.77±7.99 while the duration of marriage in 29 cases (0.5-30) years, as one was divorced, with mean and SD 12.95±8.26. Comparing the result of pap smear, histopathology, colposcopy and PCR swap in diagnosis of HPV with the golden standard test ISH PCR tissue, the sensitivity were 87.5%, 100%, 62.5% and 56,2% respectively but the specificity were 78.6%, 42.9%, 28.6% and 100% respectively

This study aimed to evaluate the different methods of diagnosis of cervical HPV infection in Egyptian females by cytology, histopathology, colposcopy and HPV genotyping.This study included 30 patient with either abnormal pap smears prior to colposcopic examination (10 cases) and abnormal T Z zone on colposcopic examination (20 cases).We considered Pap smear result suggestive of the presence of HPV infection when we found (ASUS, LSIL, HSIL, koliocytic atypia).

Keyword:HPV-PCR- Histopathology- Cytology

List of Contents

List of Tables

List of Tables (Cont…)

List of Figures

List of Figures (Cont…)

List of Abbreviations

Abb.	Meaning
AIS	Adenocarcinoma in situ
ASIR	Age Standarized Incidence Rate
AHRQ	Agency for Healthcare Research and Quality
ASCCP	American Society for Colposcopy and Cervical Pathology
ALTS	ASCUS/LSIL Triage Study
AGC	Atypical glandular cells
ASC	Atypical squamous cells
ASC-H	Atypical squamous cells can not exclude high grade
ASC-US	Atypical squamous cells of undetermined significance
bp	Base pairs
CIS	Carcinoma in situ
CIN	Cervical intraepithelial neoplasia
CGB	Colposcopic Guided Biobsy
CMV	Cytomegalovirus
DNA	Deoxy ribonucleic acid
DES	Diethylstilbestrol
DB	Dot blot hybridization
ECC	Endocervical curettage
EA	Epithelial Abnormalities
FH	Filter hybridization
FAD	Flavin Adenine Dinucleotide
FDA	Food and Drug Approved
H&E	Hematoxylin and Eosin
HSIL	High grade squamous intraepithelial lesion
HR	High- risk
HHV	Human herpesvirus
HIV	Human immunodeficiency virus
HPV	Human papilloma virus

List of Abbreviations (Cont…)

Abb.	Meaning
HC	Hybrid capture
ISH	In situ hybridization
LBC	Liquid base cytology
LSIL	Low grade squamous intraepithelial lesion
LR	Low- risk
LGT	Lower genital tract
NPV	Negative predictive Value
NADH	Nicotinamide Adenine Dinucleotide
OCT	Optical Coherence Tomography
ODS	Optical Detection System
Pap smear	Papanicolaou smear
PCR	Polymerase chain reaction
PPV	Positive Predictive Value
RCI	Reid Colposcopic Index
pRB	Retinoblastoma gene product
STH	Southern transfer hybridization
SCJ	Squamocolumnar junction
SCC	Squamous cell carcinoma
TZ	Transformation zone
URR	Upstrea regulatory region
VIA	Visual Inspection of the cervix after Acetic acid
VILI	Visual Inspection with Lugol's Iodine
VIAM	Visual Inspection with Magnification

INTRODUCTION

Cervical cancer is recognized as the third most common type of cancer in women worldwide and the second most prevalent cancer type and cause of cancer-related mortality in women in developing countries ***(Jemal et al., 2011).*** High-risk human papillomavirus (HPV) infection has been established as the main cause of cervical cancer ***(Zur Hausen, 1996).***

Humanpapilloma virus is a nonenveloped DNA virus with a protein capsid. More than 120 different human papillomavirus (HPV) types have been catalogued so far, of which more than 40 infect the epithelial lining of the anogenital tract and other mucosal areas of the body ***(De Villiers et al., 2004).***

HPV types are often referred to as "cutaneous" or "mucosal" types. In general, cutaneous types infect the keratinizing epithelium (especially the skin of the hands and feet), while mucosal types infect non keratinizing epithelium, primarily the anogenital tract epithelium, though they can also be found in the oral mucosa, conjunctiva and respiratory tract ***(Bonnez & Reichman, 2000).***

Clinically, HPV types are classified as high-risk (HR) or low-risk (LR) based upon their cervical cancer oncogenicity, Low-risk HPV types **6** and **11** cause nearly all genital warts and a minority of subclinical HPV infections ***(Bosch et al., 2002).*** In contrast, the high-risk HPV types include 16, 18, 31, 33, 35, 45, and 58 and account for approximately 95 percent of cervical cancer cases worldwide. Other high-risk HPV types less often associated with neoplasia include 39, 51, 52, 56, 59, 68, 73, and 82 **(*Munoz et al., 2003).***

Transmission of genital HPV usually requires sexual contact with the genital skin, mucous membranes, or body fluids of a partner with either warts or subclinical infection ***(ACOG, 2005).***

The variation of cervical lesions induced by HPV infection is involved in the continuous pathological process, including the subclinical, latent, and persistent infection of high risk (HR)-HPV, chronic cervicitis with abnormal results of cytological examination, cervical intraepithelial neoplasia (CIN), and cervical cancer, The majority of women with HPV infection do not develop into cervical cancer, which indicates that the single factor of HPV infection may be not sufficient for carcinogenesis ***(Shuang et al., 2010).***

The well-known risk factors of HPV infection in cervical lesions consist of high-risk sexual behaviors, immunosuppressant, age, contraceptive methods, other concurrent infection of sexually transmitted diseases ***(Deacon et al., 2000).***

The relationship between HPV genital infection and CIN and cervical lesions was first proposed by German virologist Zur Hausen in the early 1980s ***(Shuang et al., 2010 & Zur Hausen, 2000).*** It was reported that the detection rate of HPV infection in normal women, patients with CIN I, CIN II, CIN III, and cervical cancer was 4%, 30%, 55%, 65%, and 99.8%, respectively ***(Kulasingam et al., 2002).***

Infection with HPV is suspected by the appearance of clinical lesions and through the results of cytology, histology, and colposcopy, all of which are subjective and often inaccurate. In addition, serology is unreliable and unable to distinguish past from current infection ***(Carter, 2000).***

HPV infections are the most common diagnosed sexually transmitted diseases today. Studies utilizing HPV DNA testing of asymptomatic women in the general population estimate the prevalence of HPV infection to be in the range of 2–44% ***(Herrero et al., 2005).***

This wide variation in prevalence estimates is largely explained by age differences among population samples studied, and by differences in the molecular sensitivity of the various HPV DNA assays used to detect viral DNA ***(Bosch, 2003).***

Papanicolaou (Pap) staining is the gold standard for detecting abnormal cervical epithelial cells, using microscopic analysis of conventional cervical smears or cell suspensions from liquid cytology medium ***(Molijn et al., 2005).***

Molecular diagnostic tests for HPV can augment screening for cervical cancer when used in conjunction with the Pap smear ***(Molijn et al., 2005).***

Colposcopy is one of the primary diagnostic methods used to detect CIN and cervical cancer, following an abnormal cytological screen (Papanicolaou smear) so the major role of colposcopy is in guiding the diagnostic biopsy. Fundamentally, the clinicians in the United States follow a histological standard of disease, in which the histological diagnosis of the colposcopically directed biopsy is considered the true underlying disease severity. This severity dictates management ***(Jeronimo & Schiffman, 2006).*** HPV testing changes the colposcopic practice as HPV screening and triage will increasingly change the patient population referred to colposcopy ***(Jeronimo & Schiffman, 2006).***

AIM OF THE WORK

Evaluation of the different methods of diagnosis of cervical HPV infection in Egyptian females by cytology, histopathology, colposcopy and HPV genotyping.