

**SERUM CANCER ANTIGEN 125 (CA 125) LEVEL
IN PATIENTS WITH
FLAT CERVICAL CONDYLOMA**

THESIS

Submitted for partial fulfilment of
Master Degree in Obstetrics and Gynecology

BY

EMAD FEKRY GIRGIS

M.B. .B.Ch.,

Faculty of Medicine, Ain Shams University.

SUPERVISORS

Prof. Dr. MAHMOUD ALI EL-SHOURBAGY

*Professor of
Obstetrics and Gynecology
Ain Shams University*

Prof. Dr. ALI KHALIFA ALI

*Professor of
Biochemistry
Ain Shams University*

Dr. MAGED MOHAMED ABOUSEEDA

*Lecturer of
Obstetrics and Gynecology
Ain Shams University*

**FACULTY OF MEDICINE
AIN SHAMS UNIVERSITY**

CAIRO

1990

**SERUM CANCER ANTIGEN 125 (CA 125) LEVEL
IN PATIENTS WITH
FLAT CERVICAL CONDYLOMA**

THESIS

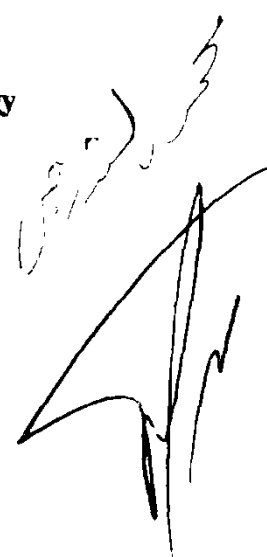
**Submitted for partial fulfilment of
Master Degree in Obstetrics and Gynecology**

BY

EMAD FEKRY GIRGIS

M.B., B.Ch.,

Faculty of Medicine, Ain Shams University.



SUPERVISORS

Prof. Dr. MAHMOUD ALI EL-SHOUBAGY

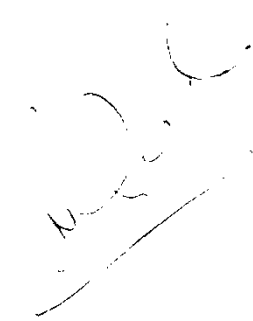
*Professor of
Obstetrics and Gynecology
Ain Shams University*

Prof. Dr. ALI KHALIFA ALI

*Professor of
Biochemistry
Ain Shams University*

Dr. MAGED MOHAMED ABOUSEEDA

*Lecturer of
Obstetrics and Gynecology
Ain Shams University*



**FACULTY OF MEDICINE
AIN SHAMS UNIVERSITY**

CAIRO

1990



TO MY MOTHER

ACKNOWLEDGMENT

I would like to express my sincere appreciation and my deep gratitude to Prof. Dr. Mahmoud A. El-Shourbagy, Professor of Obstetrics and Gynecology, Faculty of Medicine, Ain Shams University, for his fatherly valuable guidance, continuous unfailing encouragement, and kind supervision which all facilitated the performance of this work.

Also, I want to express my profound gratitude to Prof. Dr. Ali Khalifa Ali, Professor of Biochemistry and Head of Oncology Diagnostic Unit, Faculty of Medicine, Ain Shams University, for his expertise supervision and helpful advice during the work of this thesis.

May I also express my deep thanks and respect to Dr. Maged M. Abouseeda, Lecturer of Obstetrics and Gynecology, Faculty of Medicine, Ain Shams University, for his valuable cooperation.

I would like to thank, deeply, all the doctors and members of both the Cytodiagnostic Unit and Oncology Diagnostic Unit, Faculty of Medicine, Ain Shams University, for their kind help, especially Dr. Iman M. El-Salahy who helped me in laboratory procedures.

Finally, I have to thank Dr. Ibrahim Youssef for computer typing work.

CONTENTS

INTRODUCTION.....	1
AIM OF THE WORK.....	3
REVIEW	
-HUMAN PAPILLOMAVIRUS.....	4
-Tissue effects of HPV infection.....	7
-Methods of detection of genital human papillomavirus infection.....	9
-Prevalence of cervical HPV infection.....	22
-Epidemiology of HPV infection.....	24
-Clinical manifestations and natural history of HPV infection.....	27
-Cervical HPV infection - intraepithelial neoplasia - cancer as continuum.....	39
-Site - and cell - type specificity of HPV.....	42
-Role of other cocarcinogens in cancer development with HPV infection.....	46
-Correlation between lesion morphology with diagnostic grade and nuclear DNA content (cell ploidy).....	49
-Immunological reactions against HPV.....	52
-Anogenital papillomavirus infection and neoplasia in immunodeficient women.....	55
-Carbon dioxide laser therapy.....	57

-The use of topical 5-fluorouracil in the treatment of genital condyloma.....	59
-Role of interferon.....	59
-Fetal affection of genital condyloma in pregnant women....	60
-Future speculations.....	61
-TUMOR MARKERS.....	62
-Classification of tumor markers.....	64
-Structural tumor markers.....	65
-Biochemical tumor markers.....	66
-Clinical applications of tumor markers.....	81
-Tissue markers.....	84
-Histopathological applications of tumor markers.....	86
-CANCER ANTIGEN 125.....	89
-Clinical applications of serum CA 125 as a tumor marker in different conditions.....	95

SUBJECTS AND METHODS

-Subjects.....	109
-Methods.....	110
-Clinical data of the studied subjects.....	114
-Laboratory procedure.....	130
-The statistical studies used for calculation.....	136

RESULTS.....	139
--------------	-----

DISCUSSION.....	144
-----------------	-----

CONCLUSION.....150

ENGLISH SUMMARY.....151

REFERENCES.....153

APPENDIX

ARABIC SUMMARY

INTRODUCTION

INTRODUCTION

Unraveling the human papillomavirus (HPV) story has been very much a phenomenon of the 1980s. By 1988, more than 50 distinct HPV types had been characterized (Nuovo et al., 1988).

Human papillomaviral infection of the uterine cervix is one of the commonest sexually transmitted diseases with prevalence rate varying between 2-3% of the smears obtained from the normal population (Meisels et al., 1981).

It is generally accepted that most HPV cervical infection is subclinical becoming visible only during colposcopy after the application of acetic acid (Reid et al., 1980). "Flat cervical condyloma" is considered the subclinical cervical HPV infection (Meisels and Fortin, 1976).

Oncogenic HPV types could be detected in 80-90% of cervical intraepithelial neoplasia grade III lesions (Fuchs et al., 1987). Also, flat cervical condyloma induced by those oncogenic HPV types (HPV -16, -18, -31) generally show a severe degree of cervical intraepithelial neoplasia (Crum et al., 1985).

On the other hand, the consistent association between HPV infection and anogenital cancers in general, emphasizes that the sexually transmitted papillomavirus may have a necessary role in anogenital carcinogenesis.

Cancer antigen 125 (CA 125) is one of the tumor-associated antigens and it is associated with more than 80% of epithelial ovarian neoplasms of serous, endometrioid, clear cell, and undifferentiated types (Kabawat et al., 1983a). High serum levels were also observed in adenocarcinoma of the endometrium and endocervix (Niloff et al., 1984a). Bast et al. (1983) detected elevated CA 125 levels in 29% of patients with non-gynecological cancers including cancer pancreas, stomach, and breast.

So long as CA 125 levels may rise in sera of patients with some non-neoplastic conditions and some benign conditions as peritonitis and liver cirrhosis (Ruibal et al., 1984), endometriosis and fibroids (Simmonds et al., 1986), and even during menstruation (Pittaway and Fayez, 1987), it is reasonable to suspect its possible rise in some conditions which might be precancerous such as flat cervical condyloma induced by HPV infection of the uterine cervix.

AIM OF THE WORK

AIM OF THE WORK

The aim of this study is the measurement of the serum level of cancer antigen 125 (CA 125) by radioimmunoassay (RIA) among patients with flat cervical condyloma diagnosed by cervicovaginal smear, colposcopy and histopathological examination of cervical punch biopsy which might be a tool for early diagnosis or follow up in such conditions.

REVIEW

HUMAN PAPILLOMAVIRUS

I-Introduction:

The existence of the classical venereal wart (Condyloma acuminatum) in the uterine cervix had been recognized and described in details many years ago (Pitkin and Kent, 1963).

A complete reappraisal of the cervical condyloma had been made by Meisels and Fortin (1976) when the cytological and histological pattern of a new entity quite distinct from the classical condyloma acuminatum was described and known subsequently as "flat cervical condyloma".

Estimates of HPV-DNA in exfoliated cervical cells were as high as 10-20 % of sexually active population in comparison to genital herpes affecting only 1 % of this type of population (Broker, 1987).

II-Oncogenicity of HPV:

The viral DNA has been molecularly cloned from cutaneous and mucosal squamous proliferations of diverse morphology and anatomic locations and a wide range of epithelial diseases have been associated with HPV including: virtually all cases of condyloma, intraepithelial neoplasia and squamous carcinoma of both male and female lower genital tract - laryngeal and oropharyngeal papillomas - and a proportion of adenocarcinomas of the genital and oral mucosa (Zur Hausen et al., 1985 and Syrjänen, 1986).