

Table of Contents

INTRODUCTION	1
AIM OF THE WORK	3
REVIEW OF LITERATURE	4
CERVICAL CARCINOGENESIS	4
1. <i>Viruses</i>	4
a) Human papillomavirus	4
b) Herpes Simplex Virus type 2 (HSV2)	5
c) Human immunodeficiency virus (HIV)	6
2. <i>Cellular Oncogenes</i>	6
a) Ras oncogene	6
b) C myc	7
c) P53 tumor suppressor gene	7
3. <i>Cigarette smoking</i>	7
4. <i>Oral contraceptives (OCP)</i>	7
5. <i>Nutritional and dietary factors</i>	8
HUMAN PAPILLOMAVIRUS	9
<i>Physical and Chemical Properties</i>	10
Structure	10
Genome	10
Virus coded proteins	13
Transcriptional control and replication of HPV :-	15
Types of Papillomaviruses	17
Epidemiology of HPV	19
Pathological Aspects of Anogenital HPV	22
Oncogenicity of Papillomavirus	24
Human Papillomavirus and Transformation	26
HPV E7 oncoprotein	27
HPV E6 oncoprotein	29
Common mechanisms of transformation by DNA tumor viruses	30
<i>Detection and Diagnosis of HPV</i>	34
(1) <i>Cytological and histological detection</i>	34
(2) <i>Culture methods</i>	35
(3) <i>Immunohistochemical methods</i>	35
(4) <i>Electron microscopy</i>	36
(5) <i>DNA in situ hybridization "ISH"</i>	36
IN SITU HYBRIDIZATION	37
Theory or Principals of ISH	40

Probe making:	40
Probe labeling:	40
Methods of Hybridization	42
Methodology	45
Practical Application of "ISH"	49
ONCOGENESIS	53
<i>Oncogenes</i>	54
<i>Nomenclature:</i>	55
<i>Mechanisms of oncogene activation</i>	55
1- Gene amplification	56
2- Structural alteration	56
3- Loss of Control Mechanisms	58
GTP binding proteins	64
The G protein	68
Non receptor associated tyrosine kinases	68
<i>Tumor Suppressor Genes</i>	72
Nomenclature	73
Identification of tumor suppressor genes	73
Inactivation of tumor suppressor genes	75
Retinoblastoma tumor suppressor gene	77
Wilm's tumor "WT1" suppressor gene	82
Familial adenomatosis polyposis "FAP"	84
Neurofibromatosis type I "NF1"	85
Deleted colorectal carcinoma (DCC)	86
P53 tumor suppressor gene	86
MATERIAL AND METHODS	95
CASES	95
CONTROL	95
METHODS	96
KITS	96
EQUIPMENTS	98
METHODOLOGY	98
STAINING PROCEDURE	98
A) <i>In situ hybridization technique</i>	98
I) Slide preparation	98
II. Test procedure	99
Quality control	104
B) <i>P53 immunohistochemical detection</i>	104
Basic steps	104
Methods of immunostaining	105
* Interpretation of immunostaining	107
C- <i>Spectrophotometric analysis of DNA</i>	107
<i>Evaluation of DNA content in cells</i>	108
STATISTICAL METHODS	111

RESULTS	113
IN SITU HYBRIDIZATION RESULTS.....	115
<i>I. Control group:</i>	<i>115</i>
<i>II Cervical squamous cell carcinoma group.</i>	<i>115</i>
P53 TUMOR SUPPRESSOR GENE RESULTS	126
<i>I. Control group.</i>	<i>126</i>
<i>II. Cervical squamous cell carcinoma cases</i>	<i>126</i>
DNA CYTOPHOTOMETRIC RESULTS.....	134
<i>(1) Control group.....</i>	<i>134</i>
<i>(2) The cervical carcinoma group.</i>	<i>134</i>
<i>Histograms of different tumor stages</i>	<i>152</i>
DISCUSSION.....	160
SUMMARY.....	170
CONCLUSION.....	173
REFERENCES.....	174
Arabic Summary.....	203
