UNIVERSITI TEKNOLOGI MARA

PATTERN OF P16 IMMUNOHISTOCHEMICAL STAINING IN CERVICAL TISSUES

MUHAMMMAD AFIF BIN MUNSHI

Thesis submitted in partial fulfillment of the
requirements for the degree of
Masters of Pathology
(Anatomical Pathology)

Faculty of Medicine

June 2021

ABSTRACT

Cervical cancer has been one the most common cancers affecting women worldwide. It represents a significant burden on the health care system as well as affecting the lives of patients and carers. The most frequent types of cervical cancers are adenocarcinoma and squamous cell carcinomas and while their precursors are known, the main challenge is in identifying and accurately diagnosing these precursor lesions. A well-established pitfall is the inconsistency and discrepancies that exist in diagnosing these precursor lesions. The use of p16 may help to reduce the inter and intra-observer discrepancies among pathologists. This immunohistochemistry, p16 serves as a surrogate marker and its overexpression is detected when cells are infected by high risk Human Papillomaviruses (HR-HPV). This research aims to compare p16 expressions between normal cervical tissues, inflamed cervical lesions, metaplastic cervical lesions, low and high grade cervical intraepithelial neoplasia and malignant epithelium and analyze the significant difference between them. The cases are taken from records of Anatomic Pathology Unit, Faculty of Medicine, Universiti Teknologi MARA which provides diagnostic services for patients from Hospital Sungai Buloh and Clinical Training Centre, Faculty of Medicine, Universiti Teknologi MARA. A total of 20 samples from each category; normal cervix (n=20), cervicitis (n=20), cervical metaplasia (n=20), low grade CIN (n=20), high grade CIN (n=20) and invasive cervical carcinoma (n=20) were studied. The immunohistochemical staining with p16 were done on all the cases and interpreted using the Allred scoring system and block staining method. The results showed a significant difference in the uptake of the p16 staining pattern between cervical cancer, high grade cervical intraepithelial neoplasia and low grade cervical intraepithelial neoplasia. A chi square test was used to analyze the result and the obtained p value was < 0.05. In conclusion, due to the different expressions of p16 in different types of lesions in the uterine cervix, p16 is a helpful marker in the diagnosis of cervical pathology

ACKNOWLEDGEMENT

Firstly I would like to thank God for giving me the opportunity to embark on my Masters and for completing this long and challenging journey successfully. My gratitude and thanks to my supervisor Dr Norsalmah binti Bakar and co-supervisor Assoc.Prof Dr Noor Kaslina Mohd. Thank you for the support, patience and ideas in assisting me with this project. I also would like to express my gratitude to the staff of (CPDRL) for providing the facilities, knowledge and assistance.

Finally this thesis is dedicated to my parents and my wife who have given me strength and ongoing encouragement throughout the whole Masters Programme.

TABLE OF CONTENTS

CHAPTER 1
INTRODUCTION

1.1 Background of the study

Cervical cancer is a leading cause of morbidity and mortality worldwide, with an estimated incidence of 470,000 [WHO,2006]. Despite numerous screening programmes to detect early pre-cancerous changes of the cervix, cervical cancer remains an important health issue among women worldwide. Cervical cancer is the fifth (3.7%) common cause of cancer following prostate (7.9%), colorectal (9.7%), breast (11.9%) and lung cancer (13.0%) globally. It is the fourth (7.9%) common cause of cancer among women after breast (25.2%), colorectal (9.2%) and lung cancer (8.8%). Seventy percent of cervical cancer cases occur in low resourced countries (Torre, Bray, Siegel,et al, 2015). The differences in incidence are attributed mainly to the utilization of cytological screening in numerous industrialized countries during the latter half of the 20th century [Gustafsson, Pont´en, Zack, Adami,1997]. Cervical cancer is the second most common cancer among women in Malaysia (Zaridah, 2014). The age-standardised rate is highest among Indians (10.3/100,000) followed by Chinese (9.5/100,000) and Malays (5.3/100,000). The rate increases after 30 years of age and peaks at 65 - 69 years. Among all cancer deaths, cervical cancer ranked fifth (Omar, Tamin, 2011). The primary cause of cervical cancer is infection by high risk types of Human Papilloma Virus (HPV) which is transmitted sexually.

A definitive diagnosis of cervical cancer is made by histopathological examination of cervical tissue (CPG Malaysia, 2015). The two most common cervical cancers are squamous cell carcinoma followed by adenocarcinoma comprising approximately 70% and 10-25% of overall cervical malignancies in developed countries (WHO 2014). Cervical squamous cell carcinoma and adenocarcinoma are mostly associated with high-risk Human Papilloma Virus (HR-HPV) infections. Cervical intraepithelial neoplasia grades 2 and 3 (CIN 2 and CIN 3), also called high grade squamous intraepithelial lesions (HSIL) are known precursors for squamous cell carcinoma; while adenocarcinoma in situ (AIS) is a precursor for adenocarcinoma. With the use of immunohistochemical (IHC) stains, p16 overexpressed by HPV infected