

UNIVERSITI TEKNOLOGI MARA

**ROLE OF P40
IMMUNOHISTOCHEMISTRY
IN DIAGNOSING PRIMARY CERVICAL
SQUAMOUS CELL CARCINOMA
IN COMPARISON TO P63**

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ABSTRACT

Cervical cancer is one of the most common gynaecological tumours, with squamous cell carcinoma is the commonest histological subtype. Human papillomavirus (HPV) is an established primary cause of cervical carcinoma. p63 is proven to be of diagnostic value in cervical squamous cell carcinoma. p40 is a p63 isoform that causes p53 inactivation and is positively expressed in squamous cell carcinoma. However, there are limited data on p40 expression in cervical squamous cell carcinoma. This study aims to determine the role of p40 in diagnosing primary cervical squamous cell carcinoma and to evaluate the specificity and sensitivity of p40 in cervical squamous cell carcinoma in comparison to p63. A retrospective study was conducted in Pusat Perubatan Universiti Teknologi MARA (UiTM) Sungai Buloh, Malaysia where a total of 83 cases diagnosed as primary cervical carcinoma from January 2013 to December 2019 were reviewed and stratified into different histological subtypes. These cases were subjected to p40 and p63 immunohistochemistry staining. The data were analysed to evaluate p40 and p63 expression in cervical carcinoma, and the results of tumour immunoreactivity for both markers were compared. The results showed that p40 was strongly expressed in most cervical squamous cell carcinoma and adenosquamous carcinoma. p63 expression was also positive in cervical squamous cell carcinoma; however, variable reactivity was seen in other histological subtypes. The results also suggested that p40 is more specific but slightly less sensitive in identifying squamous differentiation than p63. These findings support the use of p40 immunohistochemistry as a potential reliable marker in diagnosing primary cervical squamous cell carcinoma.

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CHAPTER ONE

INTRODUCTION

1.1 Research Background

Cervical cancer poses a significant threat to women's health as it is one of the most frequent gynaecological malignancy worldwide. Most of the reported cases are diagnosed with advanced cervical cancers. This is due to delay in the diagnosis and inadequate access to healthcare services and treatment as cervical cancer can be prevented if diagnosed early [1]. Cervical cancer carries a significant burden in the under-developed and developing countries [2]. In Malaysia, cervical cancer is the third most common cancer in women and the second commonest cancer in women aged between 15 to 44 years [3]. The latest World Health Organization (WHO) Classification of Female Genital Tumours 2020 has classified cervical carcinomas into various histological subtypes. Squamous cell carcinoma accounts for the majority of all cervical cancers globally, while adenocarcinoma falls into second place [4]. It has been reported that adenocarcinoma is currently on the rise, especially in young females in developed countries [4].

Human papillomavirus (HPV), mainly HPV-16 and HPV-18, is a well-known primary cause of cervical cancer which can lead to squamous intraepithelial lesions (SIL) and subsequently to malignancy if not treated. High-risk HPV has the oncogenic potential with the ability to cause disturbances of the host cell cycle mechanism. E6 and E7 are HPV gene products that are thought responsible for making changes in host proteins expression, such as p53, p63 and Ki-67 [5, 6].

p63 gene, a p53 tumour suppressor gene homologue, plays a vital role in proliferation and maturation of the adult epithelial cells. It is commonly expressed in a number of tumours, including squamous cell carcinoma of the lung, head and neck, skin and cervix [7]. p40 gene is one of the p63 isoforms and has been widely used as a marker for squamous differentiation. Earlier studies have shown that p40 is superior to p63 in the identification of lung squamous cell carcinoma due to its higher specificity [7-11]. p40 expression has also been reported in other tumours, including squamous cell carcinomas of head and neck, oesophagus, urothelial carcinomas [12] and urothelial carcinomas [13]. However, p40 expression in squamous cell carcinoma of cervix has