UNIVERSITI TEKNOLOGI MARA

p53 PROTEIN EXPRESSION AND RISK FACTORS IN BREAST CANCER – A RETROSPECTIVE STUDY

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ABSTRACT

Numerous studies showed that overexpression of p53 protein may be involved in a variety of human malignancies including breast cancer. In breast cancer patients, a mutated p53 gene that encodes the p53 protein is associated with a higher risk of carcinogenesis and this study examine the potential role of p53 status in breast cancer tissues, specifically its association to established risk factors race, age, age at menarche, hormonal factors and cancer grade. The immunohistochemistry (IHC) technique was used to detect overexpression characteristics of p53 protein and the immunohistochemical results were compared with established risk factors. Analysis conducted on 111 breast tissues showed 40% (44/111) positive p53 (+) protein and 60% (67/111) non-expression p53 (-) respectively. Malay occupied nearly half the number of respondents for overexpressed and nonexpression of p53 (+,-) protein (n=53, 48%) followed by Chinese (n=30, 27%) and Indian (n=28, 25%) with no significant difference ($p > 0.05$). Overexpression of p53 (+) protein occurred in 37% (41/111) of the premenopausal age group above 40 years old and 3% (3/111) in the age group less than 40 years old ($p > 0.05$). The probability of p53 (+) protein being overexpressed in the age group less than 40 years old is 0.66 RR 0.665(CI :0.246-1.796) times less likely compared to age group above 41 years old. More than half of the women 66.7% (74/111) experienced menarche at age <13 years old. The odds OR 4.509(C.I 1.746-11.644) of overexpressing p53 (+) protein are 4.5 times more likely in menarcheal age group <13 years old compared to >13 years old. Overexpression of p53 (+) are 4.4 times more likely (OR4.363, C.I 1.44-6.848) when both hormonal receptors are positive [ER (+) PR (+)]. Women diagnosed with grade 3 breast tumours are likely to overexpressed p53(+) protein 2.8 times more (OR 2.799 C.I 1.728-11.014) than women diagnosed with breast tumour grade 1 and 2 which explained the elevated number of high risks women with poor prognosis. In conclusion, secular trend influence by early life physiological events in breast development at menarcheal age may presumably had implications in breast cancer incidence with the increased risk associated with p53(+) protein within this age group. Increased risk in coexpression [ER (+) PR(+) p53(+)] including higher grade tumours and p53(+)characterized a subgroup of patients with clinical implication. Inclusion of p53 in routine diagnostic evaluation and primary assessment may provide additional information or early evidence of predictive and prognostic significance in diagnosis, and may ultimately influence the therapeutic algorithm of premenopausal women with breast cancer.

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CHAPTER ONE
INTRODUCTION

1.1 BACKGROUND OF STUDY

This chapter is an overview of the epidemiology, risk factors, pathology, diagnosis and treatment of female breast cancer both internationally and nationwide based on cancer incidence statistics, mortality, survival, prevalence, and their trends. This chapter explores some perceptions and misconceptions of breast cancer, what shapes ones beliefs and ideas about this disease and how this impacts on current health care provision. Emphasis on the biological basis of breast cancer as well as what causes breast cancer to develop are also addressed, as it is essential that healthcare professionals understand the underlying biological changes occurring during the development of a disease in order to have a better understanding that requires management on care of the individual.

Normal Breasts, or mammary glands, function to produce milk. In normal cell cycles of proliferation and regression are controlled by hormones and growth factors. Abnormal cellular changes progress from proliferative disease to atypical hyperplasia to carcinoma in situ to invasive breast cancer. While the majority of breast cancers are adenocarcinomas occurring in the upper outer quadrant, breast cancer is a complex and heterogeneous group of diseases with distinct morphologic and molecular features (Foxson, Lattimer, 2011; Cadoo, Traina, & King, 2013; Watanabe et al., 2015). Over the past century there has been a dramatic increase in pathological abnormality cases which is referred as cancer. According to recent facts by American Cancer Society (2015), cancer is best defined as a group of diseases characterized by uncontrollable growth of abnormal cells which could spread to other part of body, and potentially to be lethal if not properly treated. Cancer has been proposed to be induced by external factors, namely tobacco and infectious agents, or by internal factors such as hormones and inherited genetic mutations. In Time magazine (2007), the editors deliberately chose to use a white woman to represent the original ‘face’ of breast cancer on its front cover. According to the accompanying article, this is because breast cancer was previously associated with white, affluent women in North America and Western