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**MATRIC NO.: 16/MHS01/168**

**COURSE: INTRODUCTION TO HISTOPATHOLOGY**

**LECTURER: EDEM EDEM**

**QUESTIONS:**

1. **Write on cancers epidemiology in Africa generally, and Nigeria in particular.**
2. **Critically examine the involvement of angiogenic genes in the development and progression of osteosarcomas**

1.

The burden of cancer in Nigeria is unknown; mainly because of lack of statistics or under-reporting. This is not peculiar to Nigeria but most parts of Africa. In a study of cancer registry literature update from all over the world, only 1% of the literature emanated from Africa compared to 34% and 42% from Europe and Asia respectively 3.

This is partly due to inaccurate population statistics which makes age specific incidence rates impossible or if available inaccurate. Large proportions of the population still never seek orthodox medical care and so are not recorded.

The earliest study from Nigeria was from the Ibadan Cancer Registry-1960-69(ICR); Edington & MacLean reported higher rates of cancer in females with age standardized rates (ASR) of 105.1 and 78 per 100,000 females and males respectively . In 1998, 74.5 per 100,000 females and 63.9 for males was recorded from the same center . In Zaria, 1976-78 data reported 1575 cases with 52% of cases in males and 48% in males; a latter study however showed more cancers in females than males (Fatima, 2009)

Analysed data from 2 population based cancer registries in Nigeria, the Ibadan Population Based Cancer Registry (IBCR) and the Abuja Population Based Cancer Registry (ABCR) covering a 2 year period 2009–2010 (Elima *et al.,* 2012). Data are reported by registry, gender and in age groups. Data presented on the age specific incidence rates of all invasive cancers and report age standardized rates of the most common cancers stratified by gender in both registries.

The age standardized incidence rate for all invasive cancers from the Ibadan Population Based Cancer Registry (IBCR) was 66.4 per 100 000 men and 130.6 per 100,000 women. In Abuja Population Based Cancer Registry (ABCR) it was 58.3 per 100 000 for men and 138.6 per 100 000 for women. A total of 3 393 cancer cases were reported by the IBCR. Of these cases, 34% (1 155) were seen among males and 66% (2 238) in females. In Abuja over the same period, 1 128 invasive cancers were reported. 33.6% (389) of these cases were in males and 66.4% (768) in females. Mean age of diagnosis of all cancers in men for Ibadan and Abuja were 51.1 and 49.9 years respectively. For women, mean age of diagnosis of all cancers in Ibadan and Abuja were 49.1 and 45.4 respectively. Breast and cervical cancer were the commonest cancers among women and prostate cancer the most common among men. Breast cancer age standardized incidence rate (ASR) at the IBCR was 52.0 per 100 000 in IBCR and 64.6 per 100 000 in ABCR. Cervical cancer ASR at the IBCR was 36.0 per 100 000 and 30.3 per 100 000 at the ABCR. The observed differences in incidence rates of breast, cervical and prostate cancer between Ibadan and Abuja, were not statistically significant (Elima *et al.,* 2012).

2.

Osteosarcoma is the most common primary malignancy of bone. It arises in bone during periods of rapid growth and primarily aﬀects adolescents and young adults, without a supporting vasculature, osteosarcoma cells would be unable to obtain the nutrients and oxygen necessary for proliferation (Mathew *et al.,* 2011).

Tumor cells, like normal cells, require the delivery of oxygen and nutrients by blood vessels in order to survive and grow. In most normal adult tissues, vessels are quiescent due to the presence of equal or higher levels of inhibitors relative to inducers of angiogenesis. In pathological angiogenesis, the balance of mediators shifts so that inducers predominate, either due to increased secretion of inducers or decreased secretion of inhibitors, or a combination of both. In initial tumor development, known as in situ carcinoma, there appears to be a prolonged dormant period during which the tumor is not angiogenic, and is restricted in growth to a few cubic millimetres (Folkman , 1971). When sufficient tumor cells have switched to the angiogenic phenotype from a quiescent phenotype, neovascularization may begin, and hence rapid tumor growth and metastasis can proceed. This process, known as the “angiogenic switch,” is complex and remains incompletely understood. It can be triggered by various signals, including metabolic stress such as hypoxia, acidosis and hypoglycemia, mechanical stress such as pressure, immune or inflammatory response, and is often a consequence of the genetic alterations that drive tumor progression. Tumors become angiogenic by increasing the local expression of pro-angiogenic factors, such as vascular endothelial growth factor (VEGF), basic fibroblast growth factor (bFGF), platelet-derived growth factor (PDGF) and transforming growth factor (TGF)-β. These factors may be mobilized from the extracellular matrix, or produced by recruited host macrophages and mast cells or the tumor cells themselves (Folkman , 1995; Dvorak *et al.,* 1991) . Tumor cells also secrete proteolytic enzymes that degrade basement membrane and extracellular matrix, thus allowing angiogenesis to proceed (Dano *et al.,* 1985). The angiogenic factors stimulate quiescent endothelial cells to degrade

and migrate into extracellular matrix, and to proliferate and organize themselves into new capillaries, (Folkman , 1992). As tumors grow, internal areas of hypoxia develop, which further stimulate production of pro-angiogenic factors (Gee *et al.,* 1999). The importance of the production of pro-angiogenic factors in osteosarcoma pathogenesis and progression has been highlighted by numerous studies that have shown VEGF expression to be correlated with increased tumor vascularity and metastatic potential, and poorer prognosis in osteosarcoma (Lee *et al.,* 1999; Handa *et al.,* 2000; Kaya *et al.,* 2000). Serum VEGF levels were five times increased in pediatric patients with malignant solid tumors, including osteosarcoma, compared to normal healthy controls (El-Houseini *et al.,* 2004). These studies advocate a role for inhibition of tumor angiogenesis using anti-VEGF methods. Other angiogenic factors such as TGF-β1 have similarly been associated with the more aggressive phenotype in osteosarcoma (Franchi *et al.,* 1998). Recent studies, however, have given conflicting results as to whether increased tumor angiogenesis is associated with worse clinical prognosis in osteosarcoma (Mantadakis *et al.,* 2001; Mikulic *et al.,*2004; Kreuter *et al.,* 2004).

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