# PRE-TREATMENT RED BLOOD CELL INDICES IN MUCOSAL HEAD AND NECK SQUAMOUS CELL CANCERS AT THE KENYATTA NATIONAL HOSPITAL, NAIROBI, KENYA

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## ABSTRACT

**Background**: There has been a growing interest in the pathologic, diagnostic, and prognostic utility of haematologic parameters in the management of Mucosal Head and Neck Squamous Cell Carcinoma (HNSCC).
**Objective**: This study sought to compare pre-treatment red blood cell indices of mucosal HNSCC to that of the general population and to correlate these with cancer characteristics of the study population.
**Design**: This was a cross-sectional case control study.
**Methods:** The study was conducted at the Kenyatta National Hospital (KNH), Nairobi, Kenya. Cases were patients aged 18 years and above, presenting with a histological diagnosis of mucosal HNSCC. Controls were healthy individuals, aged 18 years or above who were not being followed up regularly for any disease conditions. Complete blood count was analysed with an automated analyser (SYMEX™, MODEL: XN500). Comparative analysis of quantitative data was achieved with Student's T test whereas qualitative data was evaluated by using Chi-square and Fishers exact tests. Normally distributed data was analysed with one- way ANOVA test. A two tailed P-value of <0.05 was our cut-off for statistically significance.
**Results**: A total of 122 participants (61 cases and 61 controls) met the inclusion criteria. Males constituted 67.2% (41) of each study arm. The mean age for cases was 45.30±17.17 years and 43.00±15.45 for controls, (P=0.44). Laryngeal carcinoma was the most common cancer (31.1%) among our participants. Most participants (91.8%) were at advanced stage (T3 and T4) at the time of recruitment into the study. There was a significant difference in haemoglobin levels (12.5±2.5 vs 14.5±1.8, P<0.001), mean corpuscular volume (85.4±8.7vs91.6±6.3, P < 0.001), red cell distribution width (14.8±3.5 vs 13.8±1.2) and total platelet counts (409.5±139.7 vs 247.8±76.1) between HNSCC and the general population. Lowest levels of Hb and MCV were observed with more advanced tumours in terms of nodal staging, (P=0.01).
**Conclusion**: Mucosal HNSCC is significantly associated with lower values of Hb and MCV compared to the general population. The more advanced the disease, the lower the Hb and MCV values. Patients in this setting therefore need close follow up in terms of nutrition and clinical evaluation for optimal treatment outcomes.

**Key words:** Inflammation, Red blood cell, Red cell distribution width, Haemoglobin, Mucosal head and neck squamous cell carcinoma, Kenyatta National Hospital

## INTRODUCTION

Recently, the relationship between cancer and haematologic markers have become a growing field of research. Interest in the pathologic, diagnostic, and prognostic utility of haematologic parameters has expanded the understanding of the vital role they play in cancer treatment and outcomes. Changes in the haematological profiles have shown association with incidence of both pre-cancerous and malignant lesions of the head and neck region[1]. Anaemia is known to engender radio-resistance and pre-treatment Hb is an important factor determining treatment outcomes in cancers of the head and neck and other regions[2]. The pathologic mechanism relates to tissue hypoxia which directly bears upon haemoglobin as the major oxygen transfer molecule to tumour cells. Studies have shown that anaemic head and neck cancer patients tend to have low oxygen partial pressures within the primary tumours and neck node metastasis, which invariably leads to poor response to radiation therapy and poor treatment outcomes[3]. Aetiologies of anaemia in

mucosal head and neck cancer patients revolve around iron deficiency due to poor food intake, absorption and other tumour induced metabolic abnormalities. Iron is an essential micronutrient for human health due to its vital role in many metabolic processes. Variations in the levels of serum iron may be reflected as changes in parameters such as mean haemoglobin (Hb), Mean Corpuscular Volume (MCV), Mean Cell Haemoglobin (MCH), and Mean Corpuscular Haemoglobin Concentration (MCHC) and changes in Red Cell Distribution Width (RDW). Positive correlations have been shown between serum iron levels and cancer incidence and treatment outcomes in previous studies[4]. The red cell distribution width is a measure of the variation in the sizes of red blood cells (Anisocytosis). RDW is an important prognostic marker in various malignancies including HNSCC, partly because of its role as a marker of inflammation and also because it correlates with the nutritional state of these patients[5]. All these indices can be extracted from the complete blood count, which is a performed investigation worldwide for a variety of clinical conditions. To the best of our knowledge, there have been no studies in our setting, assessing the pre-treatment levels of red blood cell indices in HNSCC. Our aim was to compare the pre-treatment levels of red blood cell indices in mucosal HNSCC patients to those of the normal population. This study will provide a basis for establishment of baseline values for these haematologic parameters and provide insight into the active use of the same in monitoring and follow up of patients in our setting undergoing treatment for mucosal HNSCC.

## MATERIALS AND METHODS

This was a cross-sectional case control study conducted at the Kenyatta National Hospital (KNH), Nairobi Kenya. This study was approved by the ethics and research committee of the University of Nairobi/ Kenyatta National Hospital, protocol number P34/01/2019. Data collection tool was a specially designed questionnaire that captured demographic characteristics of the study population, cancer characteristics and the complete blood count result slip. Cases were patients aged 18 years and above, presenting with a histological diagnosis of mucosal HNSCC. Controls were healthy individuals, aged 18 years or older who were not being followed up regularly for any disease conditions. They were sampled among blood donors who had undergone assessment for fitness to donate and individuals with conditions like refractive errors or cataract followed up at KNH. They were matched with cases based on gender and age ranges established on 10 years interval. We excluded patients who have had or are currently on treatment for mucosal HNSCC such as surgery, radiotherapy, or chemotherapy and participants with diagnosed cancers of other body regions apart from mucosa of the head and neck region. Individuals with history of long-term steroid use were also excluded. Complete blood count was analysed with an automated analyser (SYMEX™, MODEL: XN500).

Data was expressed as mean, standard deviation and 95% Confidence Interval (CI). Comparative analysis of quantitative data was achieved with Student T test whereas qualitative data was evaluated by using Chi-square and Fishers exact tests. Normally distributed data was analysed with one- way ANOVA test. A two tailed P-value of <0.05 was our cut-off for statistically significance.

## RESULTS

A total of 122 participants (61 cases and 61 controls) met the inclusion criteria. Males constituted 67.2% (41) of each study arm. The mean age for cases was 45.30±17.17 years and 43.00±15.45 for controls, (P=0.44). The age distribution of the study population is depicted in Figure 1, and the gender distribution is presented in Table 1.

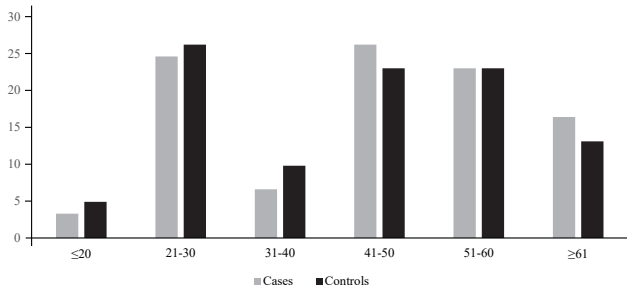


**Figure 1:** Age distribution of the study population

**Table 1:** Gender distribution

| Characteristic | Case | Control | P-value |
|---|---|---|---|
| Gender | | | |
| Male | 41(67.2%) | 41(67.2%) | 1.00 |
| Female | 20(32.8%) | 20(32.8%) | |
| Age (years) Mean | 45.30±17.17 | 43.00±15.45 | 0.44 |

Laryngeal carcinoma was the most common cancer (31.1%) among our participants (Figure 2). Most participants (91.8%) were at advanced stage (T3 and T4) at the time of recruitment into the study. Early stage presentations were relatively rare. Cervical nodal stage, N2, disease was the most encountered (49.2%) in our population. Distant metastases were found in only seven (11.5%) of participants. Well differentiated squamous cell carcinomas were seen in 31(50.8%) patients (Table 2).

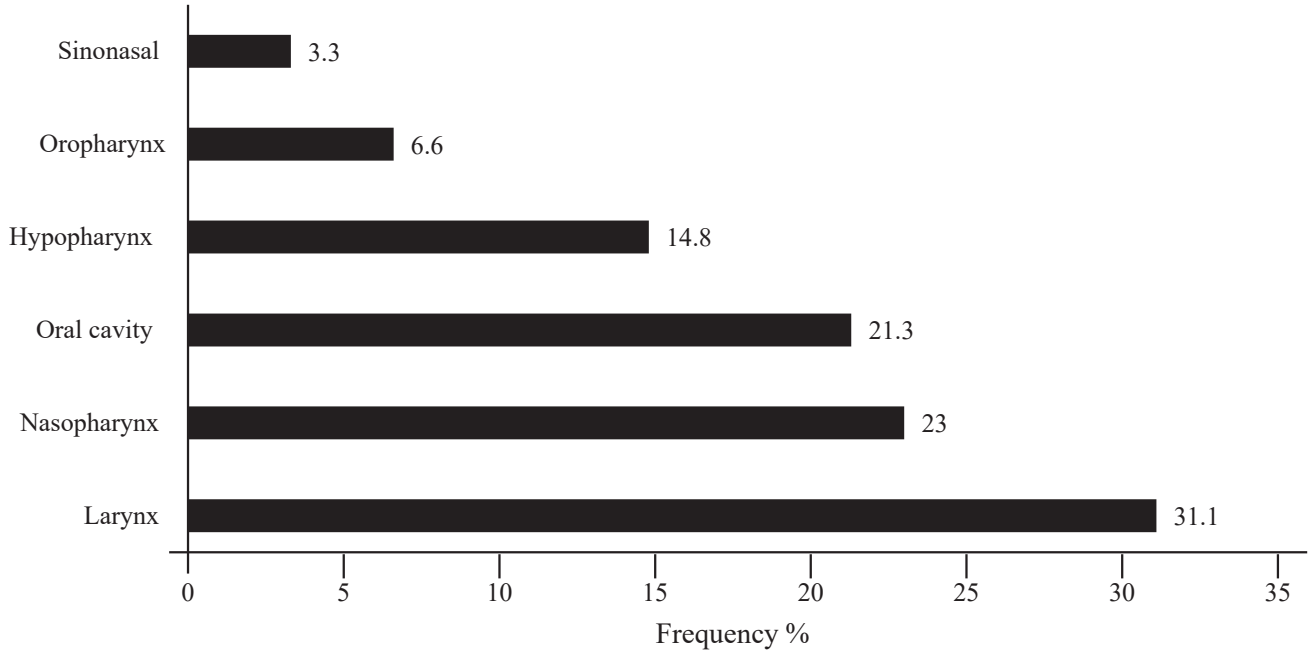


**Figure 2:** Distribution of cancers based on anatomical location

**Table 2:** Cancer characteristics

| Characteristics | | Frequency (%) |
|---|---|---|
| Location | Nasopharynx | 14 (23) |
| | Sinonasal | 2 (3.3) |
| | Oropharynx | 4 (6.6) |
| | Oral cavity | 13 (21.3) |
| | Hypopharynx | 9 (14.8) |
| | Larynx | 19 (31.1) |
| T-stage | T1 | 1 (1.6) |
| | T2 | 4 (6.6) |
| | T3 | 13 (21.3) |
| | T4 | 43 (70.5) |
| N-stage | N0 | 13 (21.3) |
| | N1 | 6 (9.8) |
| | N2 | 30 (49.2) |
| | N3 | 12 (19.7) |
| M-stage | M0 | 54 (88.5) |
| | M1 | 7 (11.5) |
| Histological grade | Grade 1 | 31 (50.8) |
| | Grade 2 | 16 (26.2) |
| | Grade 3 | 2 (3.3) |
| | Grade 4 | 11 (18.0) |

**Table 3:** Red blood cell indices

| Parameter | Normal values | Cases | Controls | P-values |
|---|---|---|---|---|
| Total red cell count | | 4.5±0.8 | 4.8±1.1 | 1.34 |
| Haemoglobin | | 12.5±2.5 | 14.5±1.8 | <0.001 |
| Mean corpuscular volume | | 85.4±8.7 | 91.6±6.3 | <0.001 |
| Mean corpuscular hemoglobin concentration | | 32.1±1.9 | 31.9±1.7 | 0.58 |
| Red cell distribution width (RDW) | 11.6-14.8 | 14.8±3.5 | 13.8±1.2 | 0.04 |
| Platelets | 142 -424 | 409.5±139.7 | 247.8±76.1 | <0.001 |

There was a significant difference in haemoglobin levels (12.5±2.5 vs 14.5±1.8, P < 0.001), mean corpuscular volume (85.4±8.7vs 91.6±6.3, P < 0.001), red cell distribution width (14.8±3.5 vs 13.8±1.2) and total platelet counts (409.5±139.7 vs 247.8±76.1) between HNSCC and the general population (Table 3). Lowest levels of Hb and MCV were observed with more advanced tumours in terms of nodal staging, (P=0.01) (Table 4).

**Table 4:** Relationship between cancer characteristics and red cell indices

| Characteristic | | Mean Hb ± SD | P-value | Mean MCV±SD | P-value | Mean RDW (CV) ±SD | P-value | Mean MCH-C±SD | P-value |
|---|---|---|---|---|---|---|---|---|---|
| Tumour location | Nasopharynx | 11.9±2.2 | 0.32 | 82.3±8.6 | 0.05 | 15.3±3.2 | 0.55 | 31.4±1.8 | 0.58 |
| | Sinonasal | 13.3±2.3 | | 80.6±4.6 | | 12.2±0.5 | | 33.5±0.6 | |
| | Oral cavity | 11.9±3.5 | | 85.6±12.0 | | 15.8±5.9 | | 32.3±2.5 | |
| | Oropharynx | 10.9±2.1 | | 78.4±4.4 | | 15.2±1.2 | | 32.9±3.5 | |
| | Hypopharynx | 13.6±2.6 | | 84.2±9.1 | | 15.1±3.3 | | 32.1±0.7 | |
| | Larynx | 13.0±1.6 | | 90.0±4.4 | | 13.8±1.5 | | 32.3±1.6 | |
| T-stage | T1 | 13.7±2.1 | 0.93 | 91.0±7.1 | 0.41 | 12.7±3.0 | 0.68 | 32.3±0.1 | 0.19 |
| | T2 | 12.6±3.1 | | 80.5±8.0 | | 15.9±3.5 | | 30.4±1.3 | |
| | T3 | 12.7±2.0 | | 88.0±7.8 | | 14.0±1.4 | | 32.8±2.3 | |
| | T4 | 12.3±2.6 | | 84.9±9.0 | | 15.0±4.0 | | 32.1±1.8 | |
| N-stage | N0 | 12.5±3.1 | **0.01** | 85.6±6.3 | **0.01** | 15.2±5.0 | 0.35 | 32.2±2.1 | 0.61 |
| | N1 | 14.8±1.5 | | 93.3±7.9 | | 13.4±1.4 | | 32.3±1.4 | |
| | N2 | 12.7±2.0 | | 86.0±7.0 | | 13.4±2.4 | | 32.4±1.9 | |
| | N3 | 10.8±2.3 | | 79.5±10.2 | | 16.2±4.5 | | 31.5±1.9 | |
| M-stage | M0 | 12.7±2.4 | 0.10 | 85.8±8.3 | 0.31 | 14.5±3.1 | 0.06 | 32.3±1.9 | 0.15 |
| | M1 | 11.0±2.2 | | 82.2±12.1 | | 17.2±5.8 | | 31.2±1.6 | |
| Histological grade | Grade 1 | 12.3±2.1 | 0.71 | 86.4±10.0 | 0.30 | 15.0±3.4 | 0.91 | 32.2±2.0 | 0.91 |
| | Grade 2 | 13.0±3.0 | | 86.2±6.3 | | 14.7±4.4 | | 32.1±1.8 | |
| | Grade 3 | 13.1±2.1 | | 75.9±2.9 | | 13.3±2.1 | | 31.4±3.6 | |
| | Grade 4 | 12.0±2.2 | | 83.0±8.00 | | 14.7±2.3 | | 31.9±1.7 | |

## DISCUSSION

This study sought to compare the pre-treatment red blood cell indices in mucosal HNSCC patients to that of the healthy population. There was predominantly male population which is consistent with the worldwide gender specific incidence rates of mucosal HNSCCs showing highest values among males than females. This is mainly attributable to cigarette smoking and alcohol consumption behaviours which are more prevalent among males than females though this trend is changing in recent years[6].

The most prevalent subtype of mucosal HNSCC was laryngeal cancer. This finding is supported by the findings of Onyango *et al*[7] in the same study setting. This is however different from other settings especially in Asia pacific region where oral cavity cancers are the most frequently encountered[6]. The difference is mainly related to the variances in risk factor exposures, where betel quid chewing is the most common form of tobacco exposure contrary to our setting where cigarette smoking predominates. Late presentation to hospital in mucosal HNSCCs is common in our setting. Our findings are similarly reported by Onyango *et al*[8] and Oburra[9] in which studies, late presentation stemmed from misdiagnosis at primary health care settings and the inefficiency of the referral system in the most part. However, presentation to health facility of mucosal HNSCCs is variable with respect to the subsite involved. Oral cavity (tongue) and glottic carcinomas generally cause early symptoms whereas pharyngeal and supraglottic tumours usually present at an advanced stage nonetheless differences in presentation times still exist from region to region.

The present study showed an extremely significant difference in haemoglobin levels and mean corpuscular volume between HNSCC and the general population[10]. Lower values of haemoglobin and MCV in head and neck cancer may suggest that iron deficiency is the underlying derangement in this population of individuals. This may implicate nutritional deficiency as the primary aetiology of anaemia as mucosal HNSCC may have a toll on food intake. However, anaemia in HNSCC may be due to variety of reasons which may or may not be related to the cancer[5]. Erythropoietin deficiency due to poor marrow function, myelofibrosis, myelonecrosis and poor dietary intake due to debility of disease may all contribute to anaemia in HNSCC. Increased RBC loss from haemorrhage or RBC destruction by haemolysis in HNSCC have been previously reported[11]. The most probable explanation for the decrease in Hb, RBC count and MCV observed in the present study is the presence of tumour induced haemolysis which in turn is related to the advanced and aggressive nature of the disease[12]. Lowest levels of Hb and MCV were observed with more advanced tumours in terms of nodal staging. These findings are important in terms of treatment of these malignancies in our setting. It has been shown that Hb level is an independent predictor of outcome of HNSCC managed with radiotherapy[13]. Negative impact of low haemoglobin levels upon response rates, local control, and survival in head and neck cancer patients treated with definitive radiation therapy have been established[13]. It is therefore imperative to optimise these group of patients prior to commencement of definitive therapy to maximise outcomes in this setting.

In conclusion, mucosal HNSCC is significantly associated with lower values of Hb compared to the general population. The more advanced the disease, the lower the Hb and MCV values. Patients in this setting therefore need close follow up in terms of nutrition and clinical evaluation for optimal treatment outcomes.

## REFERENCES


1. Bhattacharjee A, Borah FR, Sarbani G and Devnath BSU. Evaluation of hematological parameters as a possible marker for head - and - neck cancer and precancerous conditions. *J Evol Med Dent Sci.* 2015; **45**(9): 16111-16.
2. Hefler L, Mayerhofer K, Leibman B, Obermair A, Reinthaller A, Kainz C, *et al.* Tumor anemia and thrombocytosis in patients with vulvar cancer. *Tumor Biol.* 2000; **21**:309-314.
3. Becker A, Stadler P, Lavey RS, Hänsgen G, Kuhnt T, Lautenschläger C, *et al.* Severe anemia is associated with poor tumor oxygenation in head and neck squamous cell carcinomas. *Int J Radiat Oncol Biol Phys*. 2000; **15**;46(2):459-466.
4. Chua ACG, Knuiman MW, Trinder D, Divitini ML and Olynyk JK. Higher concentrations of serum iron and transferrin saturation but not serum ferritin are associated with cancer outcomes. *Am J Clin Nutr.* 2016; **104**(3):736-742.
5. Bhattathiri VN. Relation of erythrocyte and iron indices to oral cancer growth. *Radiother Oncol.* 2001; **59**(2):221-226.
6. Vigneswaran N and Williams MD. Epidemiologic trends in head and neck cancer and aids in diagnosis. *Oral Maxillofacial Surg Clin North Amer.* 2014; **26**(2):123-141.
7. Onyango JF, Awange DO, Njiru A and Macharia IM. Pattern of occurrence of head and neck cancer presenting at Kenyatta National Hospital, Nairobi. *East Afr Med J*. 2006; **83**(5):288-291.
8. Onyango JF and Macharia IM. Delays in diagnosis, referral and management of head and neck cancer presenting at Kenyatta National Hospital, Nairobi. *East Afr Med J.* 2006; **83**(4):85-91.
9. Oburra HO. Late presentation of laryngeal and nasopharyngeal cancer in Kenyatta National Hospital. *East Afr Med J*. 1998; **75**(4):223-226.

10. Adamu AL, Crampin A, Kayuni N, Amberbir A, Koole O, Phiri A, *et al.* Prevalence and risk factors for anemia severity and type in Malawian men and women: Urban and rural differences. *Popul Health Metr* [Internet]. 2017; **15**(1):12.
11. Shionoya K. A study of relationship between proliferative activity and expressed transferrin receptor content in cancer cells. *Kokubyo Gakkai Zasshi.* 1994; **61**(4):580-589.
12. Quemener V, Bansard JY, Delamaire M, Roth S, Havouis R, Desury D, *et al*. Red blood cell polyamines, anaemia and tumour growth in the rat. *Eur J Cancer*. 1996; **32A**(2):316-321.
13. Brunswick N and States U. Impact of anemia in patients with head and neck cancer. 2000; (suppl **2**):13–18.