

## ***Editorial***

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# **Management update of head neck squamous cell carcinoma**

The term head and neck cancer refers to a group of biologically similar cancer originating from the upper aero digestive tract including lip, oral cavity, nasal cavity, para nasal sinuses, pharynx (as a whole) and larynx. Although the thyroid cancer and salivary gland cancer are located in the head and neck region they are considered as separate entity because of the different clinical story, management plan and prognosis as well. Ninety percent (90%) of head and neck cancers are squamous cell carcinoma (SCCHN/HNSCC) originating from the mucosal lining of these regions.<sup>1</sup> Although HNSCC are grouped together because of broad similarity in their clinical presentation, epidemiology and aetiology, yet prognosis differs widely.<sup>2</sup>

In spite of lot of advances in the treatment of head-neck cancers (HNSCC) there has been little progress in improving survival over last few decades.<sup>3</sup> The reasons that HNSCC are diagnosed at an advance stage, requires extensive effort to determine the actual stage, requires mutilating surgery which causes further delay in taking decision. Radiation also has got limitation sometimes because of severe untoward effect and natural barriers like mandible. But the hope is that relentless effort is going on globally to conquer the obstacles.

Actual scenario about the HNSCC in Bangladesh is yet to be ascertained. We do not have any tumour registration system, but there are some sporadic studies. The author carried out a 5 years study at Bangabandhu

Sheikh Mujib Medical University (BSMMU) from 2000 to 2004 among the people coming to the OPD which reveals that 150 in 100000 (i.e. 0.15%) are suffering from HNSCC. Male was 19 per 100000 (0.19%) and female 12 per lac (0.12%).<sup>4</sup> The incidence of HNSCC shows geographical variation and time trend. They also project variation in race, age, gender and social habits. In global perspective, cancer of the oral cavity, pharynx & larynx constitute 6 percent of all cancers.<sup>5</sup> The areas of the world with high incidences are Melanesia (Papua New Guinea), Western Europe, Southern Central Asia (India and the Central Asian republics of the former Soviet Union).

In India 30% and 13% male and female respectively of all cancer suffer from HNSCC. The figure for Korea is 13.6% and 9.5% respectively.<sup>6</sup> HNSCC is responsible for 7% of all cancer patients in Australia, in USA it is around 9% and in Western Europe 10-11%.<sup>7</sup> Highest rate have been reported from Papua New Guinea, Asian part of the former Soviet Union and Western India.<sup>5,8</sup> Incidence in Bangladesh appears to be similar to India, although authors experience is that the oral carcinomas are much less common here than in the Indian population, particularly in male subjects. My study at BSMMU revealed that carcinoma of the larynx (25.22%) and pyriform fossa (20.57%) made the main component. But the main bulk was contributed by oral carcinoma, (37.70%) in female.

Regarding aetiology, the following factors have been discussed for long time i.e.

- \* Carcinogen—Tobacco, alcohol, betel nut, shada/jarda, wood dust, nickel, salted fish etc.
- \* Viruses—HPV, EBV etc.
- \* Nutritional deficiency- Iron, Vit A, Zinc (-a trace element), might have role in preventing recurrence or prolonging remission period.
- \* Genetic factors and molecular biology:

An important observation is that time trend shows direct relation with the volume and pattern of consumption of tobacco.<sup>7, 8</sup> Smoking and alcohol has got synergistic effect to each other.

Management of HNSCC starts with fixing up the stage of the disease i.e. TNM stage but biological behavior of the tumour also demands due attention. Moreover, staging advocated by UICC still has got lot of incompleteness. So each case should be considered on its own merit. Although cumbersome and sometimes requires involvement of huge expenditure, proper effort should be given to fix up the stage. The procedure, involves imaging (CT/MRI), endoscopy (Fiber optic± rigid endoscopy) in addition to clinical examination. Frozen section as well as post operative paraffin section histopathology report play role in staging (i.e. pTNM). As there is chance of individual variation in assessing the primary site and the nodes and also there is chance of stage migration because of unwanted delay in interference, surgical excision must be facilitated by frozen section biopsy.<sup>9,10</sup>

Previously didactic recommendations were made regarding the safe margin. Now it is known that margin varies with primary site and tumour. Lip cancer requires a margin of not more than 1 cm, only few millimeters of clearance are needed near the vocal cord, conversely in tongue, oropharynx and

hypopharynx 2 cm or more may be the safety line. That's why in a standard centre excision of such tumours must have frozen section facility.

If post operative radiotherapy has to be used, it should be planned on the basis of pTNM. This pTNM can be enriched by some added information like lymphatic invasion (L), venous invasion (V), residual growth (R) and grading of the tissue (G).<sup>11</sup>

Biological behavior of a tumour indicates its mode of presentation, aggressiveness etc, which depends on patients age, immune status, co-morbidity, tumour location, grading and also probably some unexplored factors.

Besides these, i.e. TNM stage and biological behavior, whether the tumour is primary or recurrence is also crucial for making decision.

In any case opinion regarding management may differ. If differs among the group of professionals (surgeon/radiotherapist), among individuals, even from centre to centre and country to country.<sup>12</sup> Obviously skill of the people concerned and existing back up support are very important. Moreover patients and family wish must be taken into account. Considering these the appropriate approach to reach the decision is to form a joint board (tumour board). This usually consists of surgical oncologist, radiation oncologist/ medical oncologist, histopathologist and sometimes social worker and other specialists like neurosurgeon, maxillofacial surgeon etc.

Plan of treatment advised by tumour board reduces the chance of incomplete treatment and/or midway deviation. This also avoids unnecessary delay in starting treatment, harassment and mishandling.

The prognosis of the patient is totally individualized. Though the target of TNM staging is to share same treatment plan and

to have same level of prognosis, the TNM staging for HNSCC is yet to fulfill.

Regarding T, arbitrariness is the main criticism, as for example: T<sub>3</sub> in carcinoma larynx having 4 criteria like fixed cord, invasion of pre-epiglottic space, post-cricoid space or medial wall of the pyriform fossa, certainly do not share the same prognosis. In buccal, pharyngeal and tongue carcinoma T staging is done on the basis of surface area but depth of the lesion is crucial for clearance and prognosis. T does not give the idea about tumour volume. Subjective variation of assessment is another limitation. N does not give the idea about the level of nodal involvement, immunological status or extra-capsular spread.

Moreover, biological behavior is yet to be incorporated in staging system. So, assessment of prognosis is yet to get a solid scientific basis.

At present the main frustrations regarding HNSCC management are:

- a) Failure of detection in the sub-clinical (pre-manifestation) stage i.e. lack of effective screening test.
- b) Quick and easy establishment of diagnosis and stage.
- c) Failure of invention of effective medical treatment.
- d) Inability to detect distal metastasis before seedling.

Autopsy reveals that, distal metastasis may develop in as much as 44% cases of carcinoma larynx that are loco-regionally apparently controlled.<sup>13</sup>

Researchers are trying to develop screening test for HNSCC. People in Eastern Virginia Medical School are screening blood sample for multiple protein biomarkers of disease and it could help to identify protein signature, specific to person having HNSCC.<sup>13</sup>

Evolution of imaging technique off course tremendously contributed in detection and assessment of HNSCC. FDG-PET can

differentiate reactionary change from malignant change in the lymph node. This also helps in detection of residual and recurrent growth.

Cytotoxic agents widely used are yet to prove their efficacy as curative in HNSCC. As an adjuvant therapy or for palliation, they are fantastic, although having side effects. But the curiosity is shifting to other modes of medical management. The nature of immune response to cancer and its potential exploitation for therapy was only recognized in the 1980s. The identification of tumour specific antigen has both diagnostic and therapeutic implications.

Detection of proto-oncogene and tumour suppressor gene opens the scope for genetic engineering.

Possible future therapeutic strategies are:

- a) Virus directed enzyme pro-drug therapy (VDEPT).
- b) Anti angiogenesis agent.<sup>14</sup>

Although relatively uncommon, HNSCC continues to be a devastating disease with high morbidity and mortality. To improve our approach to these patients following recommendation can be put forward.

- a) Develop tumour registration system.
- b) All the existing facilities should be utilized in detection and assessment of the tumour.
- c) Treatment plan must be made in a joint board (tumour board).
- d) Proper and detail documentation of clinical and operative findings must be made.
- e) Provision should be made for research on HNSCC from epidemiological and clinical aspect.

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