2. Review of Literature:

Cancer of the esophagus or head and neck can be particularly debilitating because it affects the critical functions of speech, swallowing, and breathing, as well as a patient’s appearance and social functioning (Terrell, 1999). The major inducer of oral cancer is exposure to tobacco, which is responsible for 50-90% of, cases worldwide (Reznick, et al, 2003). Difference in genetic susceptibility to tobacco-induced carcinogenesis appears to modulate an individual of squamous-cell carcinoma of the head and neck (SCCHN) (Cheng, et al, 1999)

Indeed a chronic inflammatory condition associated with increased OS (Oxidative Stress) has been suggested as one of the triggering mechanisms behind the tumor-induced immune suppression (Malmberg, et al, 2002). Recently, several studies have reported that the chronic inflammation that occurs in patients with advanced cancer may be attributable to OS, which can adversely affect the immune functions. Indeed free oxygen radicals produced by macrophages were able to inhibit nonspecific and tumor-specific cytotoxicity and down-regulate signal molecules (Kono, et al, 1996), (Bingisser, 1998). Therapeutic interventions aimed to protect the immune system in cancer patients from OS-induced cell damage may enhance their immune competence. A third mechanism may be the result of the use of antineoplastic drugs: many of them, particularly alkylating agents and cisplatin, are able to produce an excess of ROS (Reactive Oxygen Species) and therefore lead to OS (Weijl, et al, 1997). Several studies have shown that chemotherapy and radiation therapy are associated with increased formation of ROS and depletion of critical plasma and tissue antioxidants (Sabitha, et al, 1999). Thus the hypothesis may rise that the body redox systems, which include antioxidant enzymes and low molecular weight antioxidants, may be deregulated in cancer patients and that this imbalance might enhance disease progression.

Regarding the mechanisms linking OS and cachexia in cancer, the following evidence has been provided: (a) in a murine model of muscle wasting and cachexia, TNF-a has been shown to induce OS and nitric oxide synthase. Moreover, TNF-an induced cachexia could be prevented with the antioxidants D-A-tocopherol or the nitric oxide synthase inhibitor nitro-L-arginine (Buck, et al, 1996). (b) An enhanced protein
degradation is seen in skeletal muscle of cachectic mice given TNF-a, which seems to be mediated by OS. There is some evidence that this may be a direct effect and is associated with an increase in total cellular ubiquitin-conjugated muscle proteins. Another cytokine, IL-6, may play a role in muscle wasting in certain animal tumors, possibly through both lysosomal (cathepsin) and nonlysosomal (proteasome) pathways (Tisdale, et al, 2001). (c) A high rate of glycolytic activity and lactate production is commonly seen in the skeletal muscle tissue in practically all-catabolic conditions, including cancer (Shaw, et al, 1987). The treatment of cancer results in acute physiological and biochemical changes was linked with a loss of QOL. The quality of life (QOL) assessed for patients’ well-being takes into account psychological, social and physical factors. These metabolic modifications led to decreased food intake while promote wasting. Malnutrition caused due to Cancer could evolve to cancer cachexia due to complicated reactions between pro-inflammatory cytokines and host metabolism. Apart from the physical and the metabolic effects of cancer, patients usually suffered from psychological distress and severe depression (Caro, et al, 2006).

There are different types of cancer treatment for e.g. curative or palliative or supportive. The treatment process varies based on patients’ clinical conditions and nutritional status. Therefore, a patient-customized nutritional intervention was prescribed (diet counseling, oral supplements, enteral or total parenteral nutrition) according to the requirement. An early method significantly reduced or maybe reversed their poor nutritional content, improved their energy status leading to better QOL. A curative treatment coupled with nutritional intervention provided added advantage. The process enhanced tolerance and response to the oncology treatment, decreased the rate of complications and reduced morbidity by regulating the balance between energy spent and food intake. In palliative care, nutritional support increased patient's QOL by controlling symptoms such as nausea, vomiting and pain related to food intake while delaying the loss of autonomy (Caro, et al, 2006).

The review of the text confirmed that nutritional care was combined into the global oncology care because of its significant influence on QOL for a patient. In addition, the evaluation of QOL was included in nutritional support to provide sufficiency to the patient's energy needs and food intake expectations (Caro, et al, 2006).
Irradiation mucositis is an inflammatory reaction and therapeutic irradiation of the oropharyngeal mucosa, that occur in those patients who are suffering from head and neck cancer. Patients with head and neck cancer often develop serious side effect from irradiation mucositis. It has been observed that severe mucositis can cause generalized problems such as weight loss and nasogastric tube feedings. In addition, it is associated with the well-being of the patient seriously. Grading mucositis is one of the best key for the evaluation of preventive and therapeutic measures (Spijkervet, et al. 1989). The latest developments in cellular and molecular biology of mucositis has shown this process was very complex. A consistent research effort helped to understand the dynamics leading to mucosal injury and to better measures for prevention and care. The refinement of five-stage model of mucositis pathogenesis helped in the rational use of mechanical therapies to maximize the effect of these measures. Further clinical trials have determined which therapy or therapies are best, in what packages, and following what kind of care (i.e., irradiation or a particular chemotherapy regimen). Studies in nascent stage addressed these questions and to assess the effectiveness of therapeutics for prophylaxis and care of oral mucositis. The proposed clinical trials may incorporate valid evaluation systems to quantify the effects of these agents on the occurrence and severity of mucositis and mucositis-related pain, devaluation in quality of life, and treatment costs (Lionel, et al, 2006).

Newly developed mechanical agents that prevent or lessen the effect of mucositis did improve the patient functioning, energy statistics and quality of life thereby reducing treatment-related morbidity and mortality. The agent’s reduced overall healthcare costs by decreasing the need for total parenteral nutrition, further hospitalization, and opioid analgesics. Continued research of the pathogenesis of mucositis provided valuable insights of this complex debilitating disease and suggests a more practical method for clinical intervention (Lionel, et al, 2006).

Specific disease and condition-related indicators provide diagnosis of a cancer of the alimentary canal (in particular, head and neck, esophageal, gastric, or pancreatic cancers) and major complications/side effects from chemotherapy and/or radiation that primarily nullify the treatment plan of an individual already suffering from malnutrition. Some of the negative indications for enteral nutritional support included a malfunctioning gastrointestinal tract, malabsorptive conditions, mechanical
obstructions, severe bleeding, severe diarrhea, intractable vomiting, gastrointestinal fistulas in locations difficult to bypass with an enteral tube, inflammatory bowel processes such as prolonged ileus and severe enterocolitis, and/or an overall health prognosis not consistent with an aggressive nutrition therapy (Piazza-Barnett, et al, 2000). Thrombocytopenia and general pancytopenic conditions following anticancer treatments may also prevent placement of an enteral tube. Research found that oral glutamine swishes help to reduce the duration and level of impact of mucositis (Huang, et al, 2000).

The head and neck cancer patients had a significant risk for malnutrition because of dysphagia from the tumor and treatment. Patient did have problem in oral intake; however patients usually had a normal stomach and lower gastrointestinal tract. Percutaneous endoscopic gastrostomy (PEG) complements enteral nutrition support provided in the home by the patient helps to prevent weight loss, dehydration, nutrient deficiencies, treatment interruptions, and hospitalizations. It has led to lower hospital visits thereby improving the quality of life. This process requires orderly care and follow-up by a multidisciplinary nutrition management team (Raykher, et al, 2007).

Enteral feeding provides nutrients to the gastrointestinal tract by a catheter or tube. In contrast, oral feeding requires absorption of nutrients by the gastrointestinal tract. Enteral feeding is favored to parenteral feeding as the former preserves the gastrointestinal composition and prevents bacterial translocation from the digestive tract. This method has fewer complications and is less expensive than TPN. Enteral nutrition has several advantages over oral feeding, such as the ability to deliver nutrients beyond blocked areas, particularly in patients with malignancies of the oropharynx, esophagus, and stomach (Shike, et al, 1994).

Nutrients can be delivered at a slow, continuous rate, thereby permitting a longer period for nutritional absorption in patients with limited absorptive capacity. This is good in those with extensive small bowel resections and in patients with mucosal injury from chemotherapy or radiation therapy. The addition of specific nutrients to enteral feeding solutions may provide immunologic and metabolic benefits. For example are the fish oil co-3 fatty acid, glutamine, arginine, and RNA are good nutrients (Gianotti, et al, 1997).
Enteral nutrition, or tube feeding uses the digestive system, has fewer complications such as infection and organ malfunction, is often easier to administer, and is cheaper than parenteral nutrition (Piazza-Barnett, et al, 2000)(Shils, et al, 1999). In addition, nutrients are metabolized and utilized more efficiently by the body.

Traditional diets taken by mouth usually contain less than 10gm of glutamine per day. During periods of severe metabolic stress or catabolic insult 20-40gm of glutamine may be required to maintain homeostasis (Panigrahi, et al, 1997). Recent studies have shown glutamine to be more effective when administered via the enteral route (Kouznetsova, et al, 1999 & Ziegler, et al, 1990). Ready to use enteral supplements are not supplemented with glutamine because of stability issues. Standard pills or capsules are expensive and contain very small amounts of glutamine (500-1000 mg) relative to the daily dosages shown to be effective (20-30gm). Powdered glutamine is the supplement of choice because it is cost effective, easy to use, well absorbed, well tolerated, and safe (Kouznetsova, et al, 1999).

Current scientific evidence suggest that under conditions of metabolic stress glutamine is a conditionally essential amino acid needed as a fuel, to enhance nitrogen balance and protein synthesis, to boost the functioning of the immune system. Glutamine combined with antioxidants may sensitize malignant cells to therapy more effectively with the added benefit of increasing patient tolerance to doses escalating therapies (Barbar, et al, 2001). The tripeptide thiol glutamine (GSH) has facile electron-donating capacity, linked to its sulfhydryl (-SH) group. Glutathione is an important water-phase antioxidant and essential cofactor for antioxidant enzymes; it provides protection also for the mitochondria against endogenous oxygen radicals (Daniel, et al, 1997).

GSH depletion may be the ultimate factor determining vulnerability to oxidant attack. Oral ascorbic helps conserve GSH; cysteine is not a safe oral supplement, and of all the oral GSH precursors probably the last flawed and most cost-effective is NAC (N-acetylcysteine) (Parris, 1997). Glutathione exists in two forms: the oxidant “reduced glutathione” tripeptide is conventionally called glutathione and abbreviated GSH; the oxidized form is a sulfur-sulfur linked compound, known as glutathione disulfide or GSSG. The GSSG/GSH ratio may be a sensitive indicator or oxidative stress. GSH has
potent electron-donating capacity, as indicated by the high negative redox potential of the GSH/GSSG “redox couple” \( (E'0 = -0.033v) \) (Lewin, et al, 1976). It is high redox potential renders GSH both a potent antioxidant per se and a convenient cofactor for enzymatic reactions that require readily available electron pairs, the so called “reducing equivalents” (Kehrer, et al, 1994). GSH depletion can trigger suicide of the cell by a process known as apoptosis (Kehrer, et al, 1994). Depletion of glutathione in these tumor cells made them more vulnerable to the effects of anticancer drugs or the gene that promotes (CD95 or APO-1/Fas). The researchers concluded that apoptosis resistance in tumor cells depends, at least in part, on intracellular GSH level (Friesen, et al, 2004). Lowering GSH concentration may be convenient not only for the efficiency of chemotherapy, but also to induce a rather fast and direct apoptosis mechanism in tumor cells (Tormos, et al, 2004).