5. Methodology:

Subjects:
Subjects include patients with head and neck malignancies or upper GI malignancies registered in the Hospital Based Cancer Registry of Bangalore institute of oncology/ Bangalore Institute of Oncology Specialty Center and posted for primary/ adjuvant surgery.

Screening:
Volunteers for the study will be solicited using billboard flyers and tear away slips at Hospital and referrals from Oncologists in Bangalore Institute of Oncology, Bangalore.

Recruitment:
Subjects who satisfy the selection criteria and give written consent to participate in the study will be recruited through referrals from oncologists.
Subjects will be selected only if they satisfy the following selection criteria:

Selection criteria:

Inclusion criteria:
1. Patients with UGI malignancy / Head and Neck Cancer posted for surgery.
2. Indication for enteral feeding during postoperative period.

Exclusion criteria:
1. Uncontrolled diabetes
2. History of protein loosing enteropathies
3. Gout and high serum urea/uric acid level
4. Gastroenteritis
5. Diarrhea grade III and above
6. IBS (Inflammatory bowel syndrome) / Crohn’s disease
7. Should not be on any other parenteral nutrition prior to starting intervention
8. Grade III Neutropenia and above.
9. Pregnancy & Lactation
10. Creatinine level of 1.5 mg/dl or more
11. Liver dysfunction with a factor of at least 3 above the upper limit of normal in AST and ALT levels

**Trial Design:** Two arm Randomized controlled design

Study Method: Subjects with Head and Neck and Upper GI malignancies posted for surgery and satisfying the selection criteria and giving written consent will be randomized to receive L-Glutamine supplementation along with isocaloric/isonitrogenous diet or receive isocaloric/isonitrogenous diet alone via enteral route for 10 days in the postoperative period. Assessments will be done after surgery, during tenth day of postoperative period (all) and before start of adjuvant therapy to evaluate post-operative outcomes alone (see Figure 1)

**Sample Size:** In an earlier pilot study done on 12 patients in the post-operative period. There was a significant increase in GSH level following Glutamine enteral nutrition for 12 days with ES >1. Considering a conservative estimate ES as 0.8. We will need 28 subjects in each arm and considering dropout rate of 20%. We will recruit 35 subjects in each arm.

**Randomization:** Randomization will be done using computer generated random numbers. Randomization will be done using opaque envelopes with two group assignments.

**Study Outcomes:**

**Primary outcomes:**

**Secondary outcomes:**
Nutritional status as assessed using
   i) Serum albumin (Arrieta, 2010)
   iii) Anthropometry [Ht, Wt., BMI] (Hebert, et al, 2006)

Post-operative outcomes:
   i) Duration of hospital stay in days
   ii) Duration for wound healing
   iii) Duration of suture removal
   iv) Post-operative complications

Systemic Inflammatory Response
   i) Neutrophil lymphocyte ratio (Leitch, et al, 2007)

Assessment Intervals:
Assessments will be done on the day of surgery (after surgery) /before beginning the enteral nutrition and after 10 days of enteral nutrition. Patients will then be followed up for postoperative outcomes (see Table 1).

Table 1: Assessment intervals:

<table>
<thead>
<tr>
<th>Assessments</th>
<th>Post-operative day 1 (baseline)</th>
<th>Post-operative 10th day</th>
<th>Post-operative follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antioxidant status GSH</td>
<td>X</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Nutritional status</td>
<td>X</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Systemic inflammatory Response PLR/NLR</td>
<td>X</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Post-operative outcomes</td>
<td></td>
<td></td>
<td>X</td>
</tr>
</tbody>
</table>