4. CHAPTER - I

Comparison of demographic profile between normal control and sepsis patients and between the groups and their influence on the sepsis markers if any.

4.1 – General Introduction

4.2 – Study design

4.3 – Results

4.3.1 Section – A: Comparison between male and female patients in different groups.

4.3.2 Section – B: Comparison between age of the patients in different groups.

4.3.3 Section – C: Comparison between the weights of the patients in different groups.

4.4 – Discussion
CHAPTER - I

Comparison of demographic profile between normal control and sepsis patients and between the groups and their influence on the sepsis markers if any

The present study titled “Evaluation of the effects of N-acetylcysteine and vitamin C on the oxidative stress following abdominal sepsis” was conducted in the intensive care unit, of the Dept of Anesthesiology, JN Medical College and the Dept of Biochemistry, Faculty of Life Science, Aligarh Muslim University, Aligarh.

The present study was designed to compare various antioxidants defence components (enzymatic and non-enzymatic) for their potency as sepsis biomarkers, contrast them with the traditional sepsis markers and identify the most significant of them. The evaluation was done by comparing the levels of haematological and biochemical markers (proposed biomarkers and CRP) in all the sepsis patients together (n = 60) with that of the normal control (n = 15) subjects.

We also investigated the relationship between the levels of sepsis markers with the severity of sepsis. This was analyzed by initially assessing the severity of sepsis by APACHE II scoring system and then correlating the APACHE II score to the level of the haematological and biochemical markers in sepsis patients.

Finally, we evaluated the effect of intravenous administration of antioxidant, N-acetylcysteine, vitamin C and a combination of N-acetylcysteine with vitamin C on the sepsis markers and compared its effect with that of placebo control subjects.

4.1 GENERAL INTRODUCTION:

Majority of deaths amongst critically ill patients requiring intensive care are attributable to sepsis and its sequelae. Experimental and clinical evidence demonstrates that these patients suffer from severe oxidative stress which is responsible for the vascular pathology initiated by the uncontrolled production of ROS (Gutteridge and Mitchell, 1999). Various studies have emphasized that the production of ROS may be influenced by the physiological factors like age, sex and weight of the patient, other than the primary pathological process (Wichmann et al., 2000; Lagranha et al., 2010). In addition, measurement of free radical production is very difficult, owing to the very short lives of these substances. We therefore proposed nine biomarkers to indirectly evaluate the entity of oxidative stress in sepsis: total SH groups, LPO, SOD, catalase, GPX, GR, GST, G6PDH and LDH which are directly related to the extent of lipoperoxidative events (Bellary et al, 1994)
Keeping this in view we recorded the demographic profile of the patients (gender, age, and weight) and evaluated the effect of these parameters on the levels of various haematological and proposed biomarkers of sepsis.

This chapter deals with the demographic profile of the patients. It is divided into three sections. **Section A** evaluates the comparison between male and female patients in different groups. **Section B** demonstrates the comparison between the age of patients (mean ± SD, and range) in different groups. **Section C** highlights the comparison between the weights of patients (mean ± SD, weight range) in different groups.

### 4.2 STUDY DESIGN:

60 patients with abdominal sepsis were enrolled for the study on the basis of the inclusion and exclusion criteria. 15 elective normal patients (Group A) were also enrolled to compare their serum level of the haematological and biochemical markers with the sepsis patients. Blood was collected from the patients before the surgery / laparotomy to analyse the various biomarkers and was designated as preoperative sample. Following laparotomy/surgery the sepsis patients (n = 60) were randomized into 4 groups on the basis of the drugs (antioxidants) received. Each group comprised of 15 patients.

- **Group B (placebo control):** post surgical septic peritonitis patients received 100 ml of 5% dextrose 8 hourly for 3 days
- **Group C** - post surgical septic peritonitis patients received N-acetylcysteine @ 70 mg/kg dissolved in 100 ml of 5% dextrose 8 hourly for 3 days
- **Group D** - post surgical septic peritonitis patients receiving vitamin C @ 25 mg/kg dissolved in 100 ml of 5% dextrose 8 hourly for 3 days
- **Group E** - post surgical septic peritonitis patients received both N-acetylcysteine @ 70 mg/kg and vitamin C @ 25 mg/kg hourly for 3 days.

The sex ratio, mean ± SD and range in age and weight of the patients were recorded. The sex, age and weight of the patients were compared between normal control subjects and sepsis patients before they were randomised into different groups. After randomisation into 4 different groups they were compared with each other.

The demographic profile of the patients was compared between the normal control and the sepsis patients applying chi square test for proportions. The demographic profile of the patients between the groups was compared applying one way ANOVA.
4.3 RESULTS:

4.3.1 SECTION A: Comparison between male and female patients in normal control and sepsis groups

Among normal control patients the distribution of male was 53% and female was 47%. In patients with abdominal sepsis 53.3% was male and 46.7% was female. The distribution was comparable (p = 1, Table 1, graph 1).

After randomly dividing the sepsis patients into different groups the gender distribution in group B was 47% males, 53% females, in group C was 60% males, 40% females, in group D was 60% males, 40% females, and in group E was 47% males, 53% females. The sex distribution amongst the groups was comparable (Table 2, graph 2).
Table - 1

Distribution of male and female patients in normal control and sepsis groups

<table>
<thead>
<tr>
<th>Gender</th>
<th>Normal control group</th>
<th>Sepsis groups</th>
<th>Sig (p)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>8 (53%)</td>
<td>32 (53.3%)</td>
<td>1</td>
</tr>
<tr>
<td>Female</td>
<td>7 (47%)</td>
<td>28 (46.7%)</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>15</td>
<td>60</td>
<td></td>
</tr>
</tbody>
</table>

Results show the distribution of male and female patients in normal control and sepsis groups in percentage. The groups were comparable applying chi square test (p = 1)

Graph - 1

Distribution of males and females in normal control and sepsis groups

Results show the distribution of male and female patients in normal control and sepsis groups in percentage. They were comparable applying chi square test, p = 1
Table - 2

Distribution of male and female patients in normal control and sepsis groups

<table>
<thead>
<tr>
<th></th>
<th>Group A (Control)</th>
<th>Group B (Placebo)</th>
<th>Group C (NAC)</th>
<th>Group D (Vit C)</th>
<th>Group E (NAC + Vit C)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>8 (53%)</td>
<td>7 (47%)</td>
<td>9 (60%)</td>
<td>9 (60%)</td>
<td>7 (47%)</td>
</tr>
<tr>
<td>Female</td>
<td>7 (47%)</td>
<td>8 (53%)</td>
<td>6 (40%)</td>
<td>6 (40%)</td>
<td>8 (53%)</td>
</tr>
<tr>
<td>Total</td>
<td>15</td>
<td>15</td>
<td>15</td>
<td>15</td>
<td>15</td>
</tr>
</tbody>
</table>

Results show the distribution of male and female patients in different groups. They were comparable with each other.
4.3.2 SECTION B: Comparison between the age (mean ± SD and range) of the patients in different groups

The distribution of patients in the age range of 30-40 years, 40-50 years and 50-60 years was 26.6%, 46.8% and 26.6 %, respectively in normal control patients. Among abdominal sepsis patients the distribution was 23.3%, 38.3% and 38.3% in the age range 30-40 years, 40-50 years and 50-60 years, respectively. There was no statistically significant difference between the patient populations (Table 3, graph 3).

The age (mean ± SD) of the patients after randomly dividing them into different groups were 44.13 ± 5.66 years, 47.06 ± 7.59 years, 47.2 ± 7.68 years, 46.26 ± 9.11 years and 48.66 ± 8.36 years in Group A, Group B, Group C, Group D and Group E respectively. The difference in age was not statistically significant when compared with each other. There was no patient in the age range between 18 years to 29 years (Table 4, graph 4).
Table - 3

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Normal control group (No. of patients)</th>
<th>Sepsis groups (No. of patients)</th>
</tr>
</thead>
<tbody>
<tr>
<td>30 – 40</td>
<td>4 (26.6%)</td>
<td>14 (23.3%)</td>
</tr>
<tr>
<td>40 – 50</td>
<td>7 (46.8%)</td>
<td>23 (38.3%)</td>
</tr>
<tr>
<td>50 – 60</td>
<td>4 (26.6%)</td>
<td>23 (38.3%)</td>
</tr>
</tbody>
</table>

Graph - 3

Distribution of patients in different age groups

Results show the distribution of patients in different age range (30-40, 40-50, 50-60 years) in normal control subjects and sepsis groups. The number of patients in each age range were comparable between normal control and sepsis patients.
### Table - 4

Age of the patients (mean ±SD) in normal control and sepsis groups

<table>
<thead>
<tr>
<th>AGE (yrs)</th>
<th>Group A (Control)</th>
<th>Group B (Placebo)</th>
<th>Group C (NAC)</th>
<th>Group D (Vit C)</th>
<th>Group E (NAC+Vit C)</th>
<th>Sig 2 tailed p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean</td>
<td>44.13</td>
<td>47.06</td>
<td>47.2</td>
<td>46.26</td>
<td>48.66</td>
<td>0.24</td>
</tr>
<tr>
<td>SD</td>
<td>± 5.66</td>
<td>±7.59</td>
<td>±7.68</td>
<td>±9.11</td>
<td>±8.36</td>
<td></td>
</tr>
</tbody>
</table>

Results show the age (mean ± SD) of the patients of all the groups. The groups were compared applying oneway ANOVA. They were not significantly different. p > 0.05

**Graph - 4**

Mean (±SD) age of the patients in normal control and sepsis groups
4.3.3 SECTION C: Comparison between the weight (mean ± SD and range) of the patients in different groups

The distribution of patients in the range of 40-50 kg, 50-60 kg and 60-70 kg were 13.3%, 46.6% and 40%, respectively in normal control patients. Among abdominal sepsis patients the distribution was 10%, 43.3% and 46.6% in the weight range 40-50 kg, 50-60 kg and 60-70 kg, respectively. There was no statistically significant difference between the patient populations (Table 5, graph 5).

The weight (mean ± SD) of the patients in different groups were 56.73 ± 6.09 kg, 57.06 ± 8.53 kg, 61.6 ± 7.55 kg, 61.33 ±7.47 kg and 62.86 ± 6.64 kg in Group A, Group B, Group C, Group D and Group E respectively. There was no statistically significant difference in weight when compared with each other (Table 6, graph 6).
Results show the distribution of patients in different range of weight (40-50, 50-60, 60-70 Kg) in normal control subjects and sepsis patients. They number of patients in each range of weight were comparable between normal control and sepsis patients.
### Table 6

Weight of the patients (mean ± SD) in normal control and the sepsis groups

<table>
<thead>
<tr>
<th>Weight (Kg)</th>
<th>Group A (Control)</th>
<th>Group B (Placebo)</th>
<th>Group C (NAC)</th>
<th>Group D (Vit C)</th>
<th>Group E (NAC+ Vit C)</th>
<th>Sign 2 tailed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean</td>
<td>56.73</td>
<td>57.06</td>
<td>61.6</td>
<td>61.33</td>
<td>62.86</td>
<td>0.9</td>
</tr>
<tr>
<td>±SD</td>
<td>±6.09</td>
<td>±8.53</td>
<td>±7.55</td>
<td>±7.47</td>
<td>±6.64</td>
<td></td>
</tr>
</tbody>
</table>

Results show the age (mean ± SD) of the patients of all the groups. The groups were compared applying one-way ANOVA. They were not significantly different, p > 0.05

### Graph 6

**Mean (± SD) weight of the patients in normal control and sepsis groups**

Results show the mean ± SD weight of the patients in normal control and sepsis groups. The groups were comparable.
4.4 DISCUSSION:

There was no significant difference in the distribution of patients in gender, age (mean ± SD, range) and weight (mean ± SD, range) between normal control and sepsis patients. There was also no difference in gender, age and weight when compared between group A, group B, group C, group D and group E (Tables 1 – 6).

Previous studies have shown that the incidence of sepsis was higher in males as compared to females. The incidence of sepsis in female requiring intensive care treatment ranges from 30% to 40% of the total ICU admissions (Wichmann et al 2000; Peitropaoli et al 2000). Further, there is reduced generation of ROS by α-ketoglutarate dehydrogenase (α-KGDH) in female mitochondria. In addition there is reduced phosphorylation and increased activity of pyruvate dehydrogenase (PDH). Both of these are responsible for decreased ROS production in female in comparison to male during ischemia-reperfusion injury (Stirone et al 2005; Razmara et al, 2007; Lagranha et al, 2010).

Accordingly, female patients in our study could have been a factor in influencing the level of the markers of sepsis. However they did not influence the overall result of our study since the incidence of female patients were comparable between the normal control and the sepsis patients as well as between the patients of all the five groups.

The elderly people have increased incidences of age related chronic diseases of cardiovascular system, brain and immune system. Increased production of ROS has been documented as the major factor responsible for this. Researchers have proved that production of free radical and damage with free radical increase with age (Sohal and Weindruch, 1996; Sohal et al, 2002; Balaban et al 2005).

However, majority of the patients in our study were middle aged (40 – 50 years), and the mean age in all the five groups also ranged between 40 – 50 years. In addition the ages of the patients in all the groups were comparable. Therefore, the age of the patients in our study probably did not influence the level of markers since the free radical usually rise in the elderly age group.

There are studies showing that oxidative damage to lipids increases and antioxidant reserves decrease after nutritional intake (Cereillo et al, 1998; Mohanty et al, 2000). The increase in ROS generation after glucose ingestion suggests that nutritional intake has a role to play in causing increased reactive oxygen species load in the obese in a manner similar to that observed in normal subjects (Mohanty et al, 2000). Therefore,
nutritional intake is a major factor affecting reactive oxygen species generation and total oxidative load rather than overweight or obesity. Accordingly, the weight of the patients in the present study did not influence the results since none of our patient was obese or overweight. Further, the mean weight of our patients ranged between 50 to 69 kg and it was comparable between the normal control and sepsis patients and between the patients of all the five groups.

Therefore, the gender, age and weight of the patients can influence the level of haematological and biochemical markers in patients with sepsis. However, since the demographic profile of the patients in our study was comparable between the normal control and sepsis patients and also between the groups, it did not influence the overall result.