# AIM OF THE WORK

The aim of the work was to assess the role of resistin as a predictor of the functional outcomes in patients with severe traumatic brain injury.

# PATIENTS

The study was carried out on 48 adult patients according to a sample size done by biostatics department of High Institute of Public Health in Alexandria University. (Appendix A)

The study was carried out on 48 adult patients of both sexes who were admitted to the units of Critical Care Medicine Department in Alexandria Main University Hospital with the diagnosis of severe traumatic brain injury (GCS 8 or less).

Approval of the medical ethics committee of Alexandria faculty of Medicine, and an informed consent from the relatives of the patients were taken before conducting the study.

The patients were followed up for 14 days.

## The patients were classified into two groups according to GOS:

**Group I (favorable outcome):** 17 patients with favorable outcome (GOS 4, 5).

**Group II (unfavorable outcome):** 31 patients with unfavorable outcome (GOS 1, 2, 3).

## Inclusion criteria:

1- Patients with isolated severe head trauma (GCS 8 or less).

2- Patients requiring no surgical interventions (patients with diffuse axonal injury, brain edema, cerebral contusions, subarachnoid hemorrhage).

3- Patients who are admitted within 24 hours of trauma.

## Exclusion criteria:

1. Patients aged less than 18 years or more than 65 years.
2. Pregnant females.
3. Poly traumatized patients.
4. Co-morbidities: uncontrolled hypertension or hepatic and renal failure.
5. Patients requiring surgical interventions (extradural hematoma, subdural hematoma, intracerebral hemorrhage, skull fractures).

# METHODS

All patients included in the study were admitted to Critical Care Medicine department of Alexandria Main University Hospital with diagnosis of severe traumatic brain injury. They were assessed to fulfill criteria of inclusion. Informed consent was taken from relative of each selected patient. The approval of local ethical committe was obtained and all patients included in the study were subjected to the following:

1. **Full history including:** age, gender, history of hepatic or renal impairment with special emphasis on the onset of head trauma and the mechanism of injury and the time lapse since head injury till hospital admission.

2. **Complete physical examination including:**

   a. General look.

   b. Vital signs: Blood pressure, pulse, respiratory rate and temperature.

   c. General examination: Head, neck, chest, abdomen and extremities.

3. **Complete neurological examination and assessment using:**

   a- Glasgow Coma Score (table 1) [10] was done on admission, and repeated daily till the end of the study period (The 14th day).

   b- The Glasgow Outcome Score (Table 2) [63] was done at the end of the study (The 14th day).

   c- Sensory and motor examination and pupillary reflexes and cranial nerves examination were done.

**4. Radiological investigations including:**

   a. Cranial CT scanning was done to all patients on admission and was done for regular follow up and in special circumstances when the patient's condition had sudden unpredictable changes in his GCS in consistence with his treating plan.

   b. Full radiological and imaging studies to detect possible extra-cranial injuries that may compromise our study.

   c. Ultrasonography was done to all patients to exclude abdominal or pelvic blood collections and pregnancy in female patients in child bearing age, and if needed CT abdomen was also done.

**5. Laboratory investigations:**

- Routine laboratory investigations including: CBC, Na, K, random blood sugar, PT, PTT, INR, BUN and creatinine were done on admission and every day for correction of any changes in their values.

- Arterial blood gas analysis was done when needed.
- Serum resistin level was estimated on admission and 3rd day.(94)

**6. Management:**

All patients were treated in accordance with the ATLS (Adult Trauma Life Support) protocol and TBI treatment guidelines as follows: (50-52)

1- Airway was kept open and clean of any foreign bodies or dentures, and breathing was dealt with according to patients requirements and his GCS score value once patient fulfilled intubation criteria he was intubated, then bag-mask ventilated then connected to mechanical ventilation

2- Breathing to be adequate in accordance with ABG results and up to ventilatory support

3- Circulation: maintaining normovolemia by isotonic crystalloids or colloids according to patients needs and a central venous pressure was targeted around 10 – 12cm water using isotonic fluids, and if blood pressure was not maintained a vaso-active agent was used**.**

4- Diuretic therapy: mannitol and frusemide to control brain edema.

5- Epilepsy; to be controlled with appropriate anti-epileptics in accordance with recent guidelines for their prescription.

6- Position of the patient head to be maintained in neutral position at 30 degrees level of the head.

7- Normothermia and prevention of hyperthermia.

8- Glucose, control of hyperglycemia around 150 mg/dl at all times and prevention of hypoglycemic episodes during patient management.

9- Control of acid base balance and electrolyte balance.

10- Nutrition; providing nutrition in accordance with approved protocols for critically ill TBI patients.

11- Sedation and analgesia: All patients were sedated when on mechanical ventilation using either: Propofol as infusion at a rate of 10-40 ug/kg/min and was titrated according to patient condition, also midazolam was also used as a short acting agent for sedation at a dose of 0.5-4 mg /Kg initially and infusion of 0.02-1 mg /Kg/ h as long as needed to reduce agitation and increased ICP.

The studied patients (48 patients) were classified into two groups according to GOS:

**Group I (favorable outcome):** 17 patients with favorable outcome (GOS 4, 5).

**Group II (unfavorable outcome):** 31 patients with unfavorable outcome (GOS 1, 2, 3).

# Statistical analysis :[95]

Data were analysed using SPSS software package version 20.0 (SPSS, Chicago, IL, USA) [96]. Quantitative data were expressed using range, mean, standard deviation and median while Qualitative data were expressed in frequency and percent. Qualitative data were analyzed using Chi-square test also exact tests such as Fisher exact was applied to compare the two groups. Not normally distributed quantitative data was analyzed using Mann Whitney test for comparing the two groups. Pearson coefficient was used to analyze correlation between any two variables. P value was assumed to be significant at 0.05.

Receiver operating characteristic curves (ROC) were drawn; the areas under the ROC curves denote the prognostic accuracy of resistin.

Agreement of resistin was expressed in sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and accuracy using the following equations:

- Sensitivity = true positive/ true positive + false negative.
- Specificity = true negative/ true negative + false positive.
- PPV = true positive/ total positive.
- NPV = true negative/ total negative.
- Accuracy = true positive + true negative/ all the patients having the test.

# RESULTS

The current study was carried out on 48 adult patients of both sex; all of the patients were admitted to the Alexandria Main University Hospital and diagnosed as severe traumatic brain injury based on GCS (GCS≤8).

## The patients were classified into two groups according to Glasgow Outcome Score (GOS):

**Group I (favorable outcome):** 17 patients with favorable outcome (GOS 4, 5).

**Group II (unfavorable outcome):** 31 patients with unfavorable outcome (GOS 1, 2, 3).

## Demographic data: table (3), figures (4, 5)

The age of studied patients ranged from 20 to 57 years with a mean of 34.35 ± 11.25 years in group I, and ranged from 18 to 60 years with a mean of 37.23 ± 10.77 years in group II. There was no statistically significant difference between the two groups regarding age (p=0.389).

There were 13 males (76.5%) and 4 females (23.5%) in group I and there were 24 males (77.4%) and 7 females (22.6%) in group II. There was no statistically significant difference between the two groups regarding sex (p=1.000). It was obviously observed that the highest percentage of TBI in the two studied groups was among young adult males.

**Table (3): Comparison between the two studied groups according to demographic data**

| | Group I (n = 17) | | Group II (n = 31) | | P |
|---|---|---|---|---|---|
| **Age (years)** | | | | | |
| Min. - Max. | 20.0 - 57.0 | | 18.0 - 60.0 | | |
| Mean ± SD | 34.35 ± 11.25 | | 37.23 ± 10.77 | | $^{t}p = 0.389$ |
| Median | 32.0 | | 34.0 | | |
| **Sex** | **No** | **%** | **No** | **%** | |
| Male | 13 | 76.5 | 24 | 77.4 | $^{FE}p = 1.000$ |
| Female | 4 | 23.5 | 7 | 22.6 | |

P, p value for comparing between unfavorable and favorable; FE, Fisher Exact test; T, Student t-test; Min, minimum, Max; maximum, SD, standard deviations.

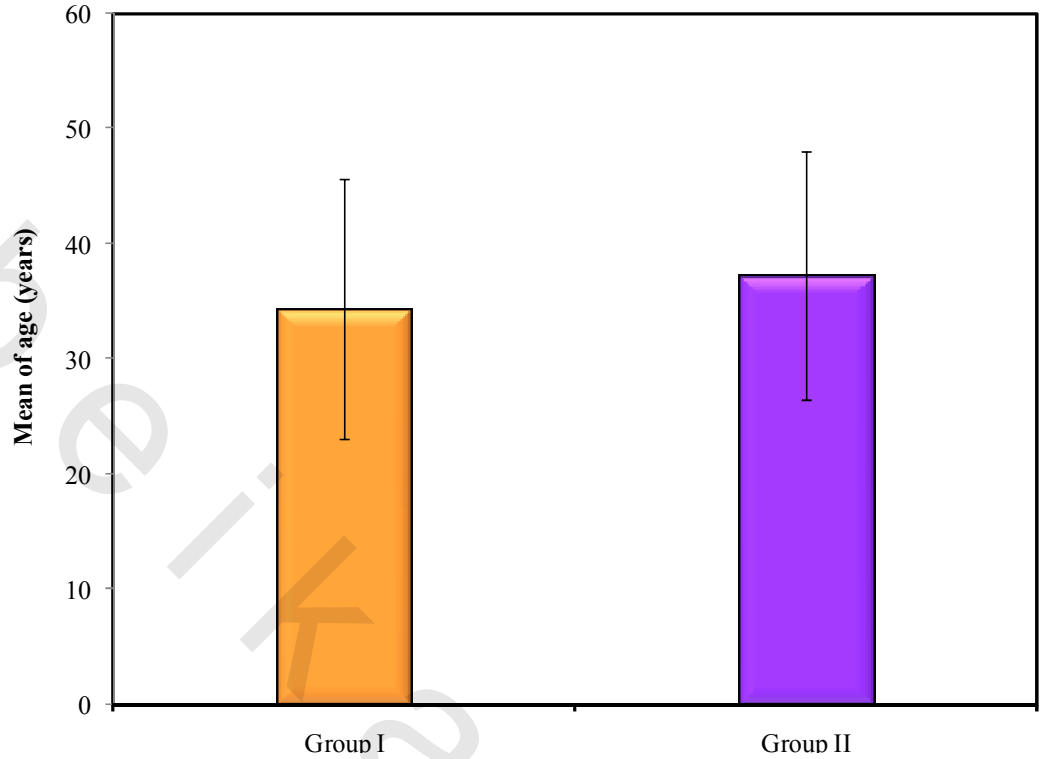


**Figure (4):** Comparison between the two studied groups according to age.

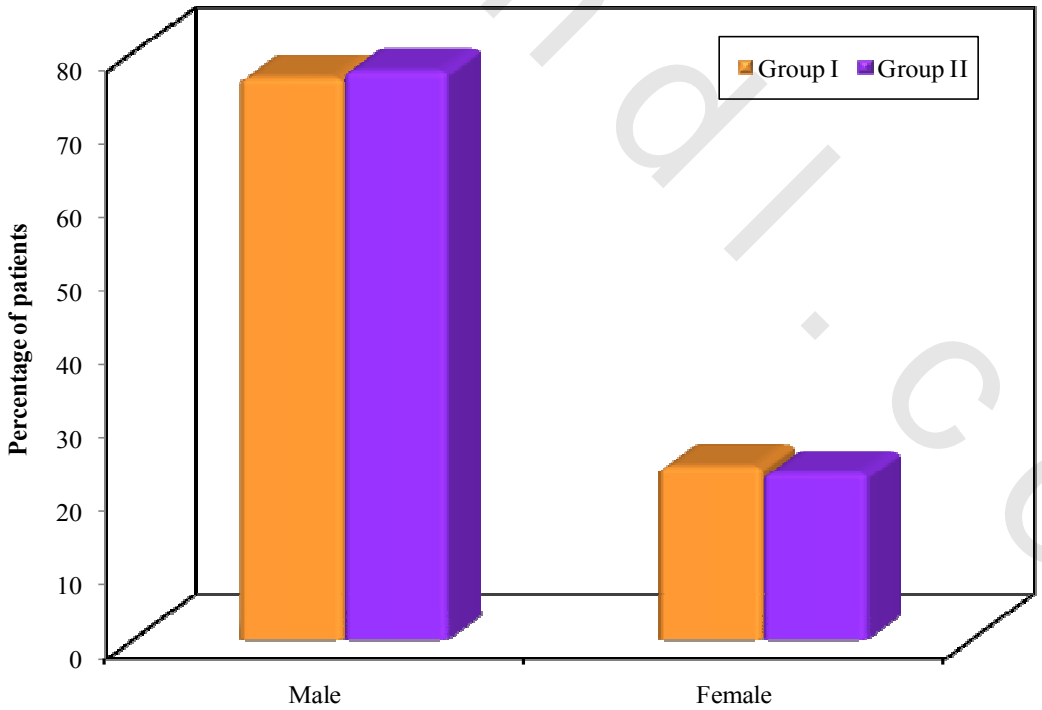


**Figure (5):** Comparison between the two studied groups according to sex.

## Mechanism of trauma: table (4) figures (6)

Road traffic accident (RTA) is the leading cause of trauma in both groups; it represents 58.8 % in group I and 74.2 % in group II, while FFH represents 29.4 % in group I and 16.1% in group II. Assault represents 11.8 % in group I and 9.7% in group II. There was no statistically significant difference between the two groups (p=0.515).

**Table (4): Comparison between the two studied groups according to cause of trauma**

| | Group I (n = 17) | | Group II (n = 31) | | P |
|---|---|---|---|---|---|
| | No | % | No | % | |
| **Cause of trauma** | | | | | |
| RTA | 10 | 58.8 | 23 | 74.2 | |
| FFH | 5 | 29.4 | 5 | 16.1 | 0.515 |
| Assault | 2 | 11.8 | 3 | 9.7 | |

P, p value for Fisher Exact test for comparing between unfavorable and favorable; RTA, road traffic accident; FFH, falling from height.

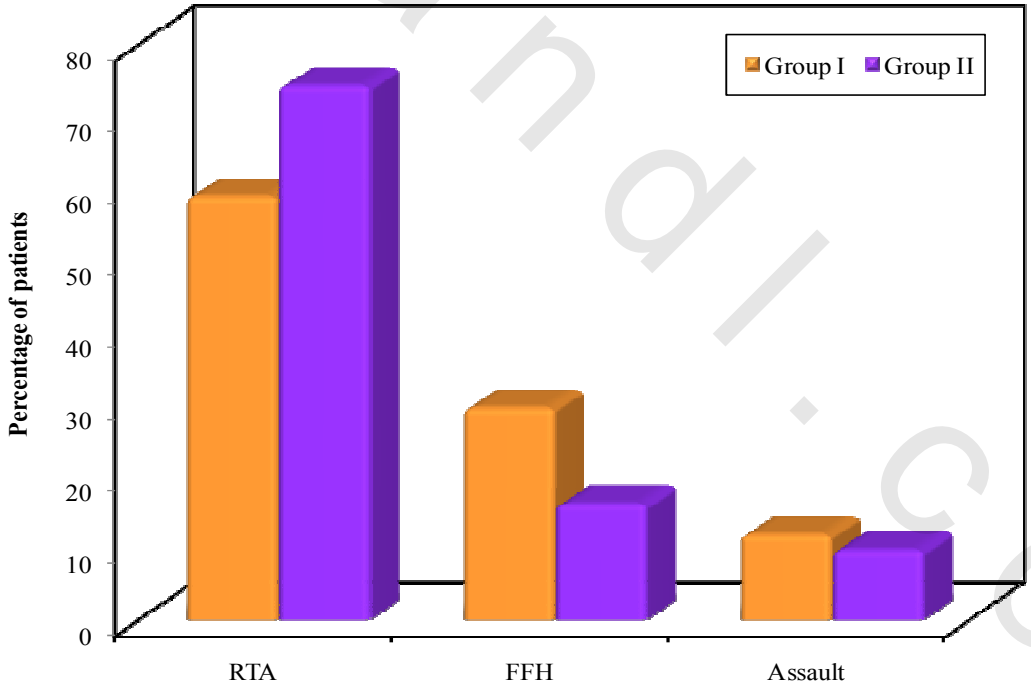


**Figure (6):** Comparison between the two studied groups according to mechanism of trauma, RTA, road traffic accident; FFH, falling from height.

## CT Brain on admission: Table (5), Figure (7)

CT brain on admission showed that in group I 29.4% of patients had brain edema, 23.5% of patients had brain contusions, 11.8% of patients had subarachnoid hemorrhage, 17.6% of patients had brain contusions plus brain edema, 5.9% of patients had subarachnoid hemorrhage plus brain edema, 5.9% of patients had subarachnoid hemorrhage plus brain contusions, 5.9% of patients had subarachnoid hemorrhage plus brain contusions plus brain edema.

In group II 9.7% of patients had brain edema, 19.4% of patients had brain contusions, 22.6% of patients had subarachnoid hemorrhage, 22.6% of patients had brain contusions plus brain edema, 12.9% of patients had subarachnoid hemorrhage plus brain edema, 6.5% of patients had subarachnoid hemorrhage plus brain contusions 6.5% of patients had subarachnoid hemorrhage plus brain contusions plus brain edema.

There was a Statistically significant difference between group I and group II regarding CT brain findings on admission (p=0.001), group II showed more hazardous findings on CT brain than group I. brain edema and brain contusions were more common in group I, while subarachnoid hemorrhage and combined lesions were more common in group II.

**Table (5): Comparison between the two studied groups according to CT Brain on admission**

| CT Brain on admission | Group I (n = 17) | | Group II (n = 31) | | P |
|---|---|---|---|---|---|
| | No | % | No | % | |
| BE | 5 | 29.4 | 3 | 9.7 | $^{MC}p = 0.001^{*}$ |
| BC | 4 | 23.5 | 6 | 19.4 | |
| SAH | 2 | 11.8 | 7 | 22.6 | |
| BC + BE | 3 | 17.6 | 7 | 22.6 | |
| SAH + BE | 1 | 5.9 | 4 | 12.9 | |
| SAH + BC | 1 | 5.9 | 2 | 6.5 | |
| SAH + BC + BE | 1 | 5.9 | 2 | 6.5 | |

MC, Monte Carlo test for comparing between unfavorable and favorable; *, Statistically significant at $p \leq 0.05$; BC, brain contusion; BE, brain edema; SAH, subarachnoid hemorrhage.

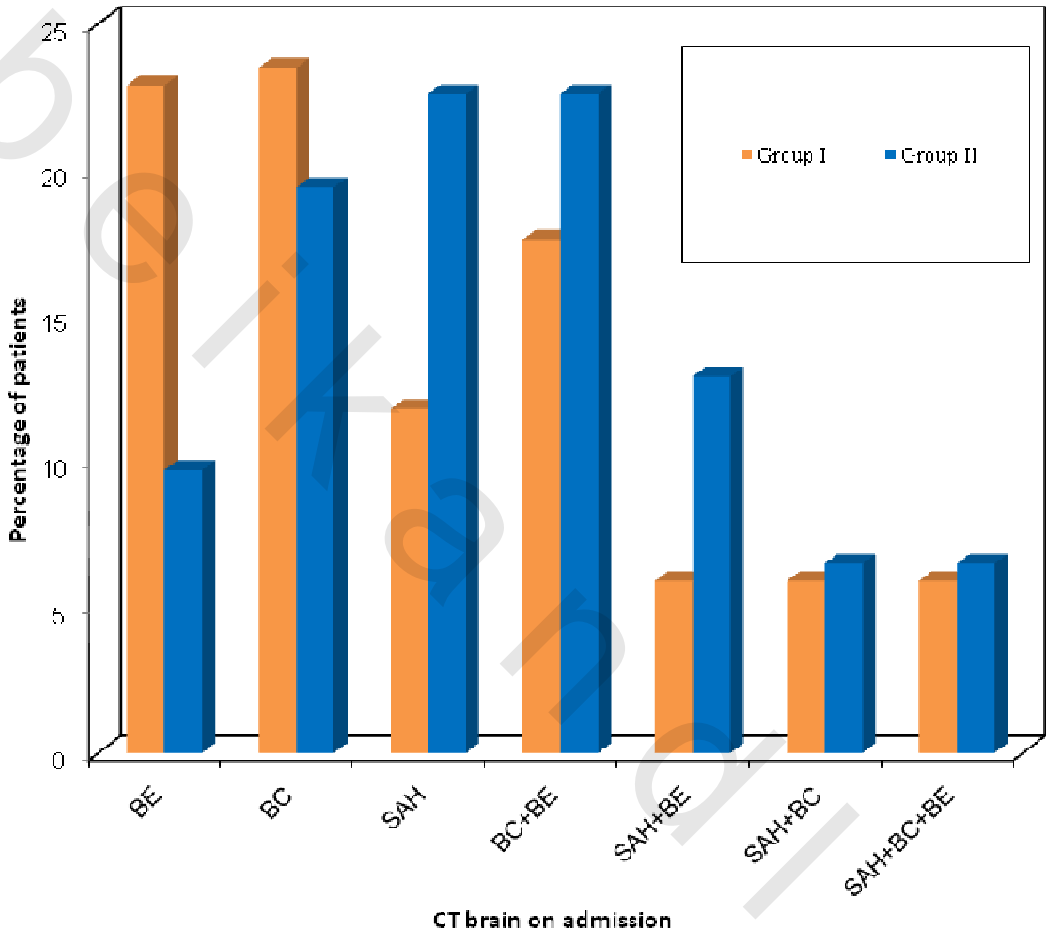


**Figure (7):** Comparison between the two studied groups according to CT Brain admission, BC, brain contusion; BE, brain edema; SAH, subarachnoid hemorrhage.

## CT Brain at the end of the study (day 14): Table (6), Figure (8)

CT brain after 14 days showed that in group I CT brain of 23.5% of patients had resolved, 29.4% of patients had brain edema, 17.6% of patients had brain contusions, 11.8% of patients had subarachnoid hemorrhage, 11.8% of patients had brain contusions plus brain edema, 5.9% of patients had subarachnoid hemorrhage plus brain contusions.

In group II 3 patients died which represented 9.7% of patients of group II, CT brain of 9.7% of patients had resolved, 12.9% of patients had brain edema, 16.1% of patients had brain contusions, 19.3% of patients had subarachnoid hemorrhage, 16.1% of patients had brain contusions plus brain edema, 6.5% of patients had subarachnoid hemorrhage plus brain edema, 6.5% of patients had subarachnoid hemorrhage plus brain contusions 3.2% of patients had subarachnoid hemorrhage plus brain contusions plus brain edema.

There was a statistically significant difference between group I and group II regarding CT brain findings at the end of the study (p=0.006). 3 patients (9.7%) were died in group II while there were no deaths in group I. CT Brain of 23.5% of patients in group I was resolved, while CT Brain 9.7% of patients in group II was resolved. brain edema and brain contusions were more common in group I, while subarachnoid hemorrhage and combined lesions were more common in group II.

**Table (6): Comparison between the two studied groups according to CT Brain at the end of the study (day 14)**

| CT Brain at the end of the study ( day 14 ) | Group I (n = 17) | | Group II (n = 31) | | P |
|---|---|---|---|---|---|
| | No | % | No | % | |
| Resolved | 4 | 23.5 | 3 | 9.7 | $^{MC}p = 0.006^{*}$ |
| BE | 5 | 29.4 | 4 | 12.9 | |
| BC | 3 | 17.6 | 5 | 16.1 | |
| SAH | 2 | 11.8 | 6 | 19.3 | |
| BC + BE | 2 | 11.8 | 5 | 16.1 | |
| SAH + BE | 0 | 0.0 | 2 | 6.5 | |
| SAH + BC | 1 | 5.9 | 2 | 6.5 | |
| SAH + BC + BE | 0 | 0.0 | 1 | 3.2 | |
| Died | 0 | 0.0 | 3 | 9.7 | |

MC, Monte Carlo test for comparing between unfavorable and favorable; *, Statistically significant at $p \leq 0.05$

BE ,brain edema; BC, brain contusion; SAH, subarachnoid hemorrhage.

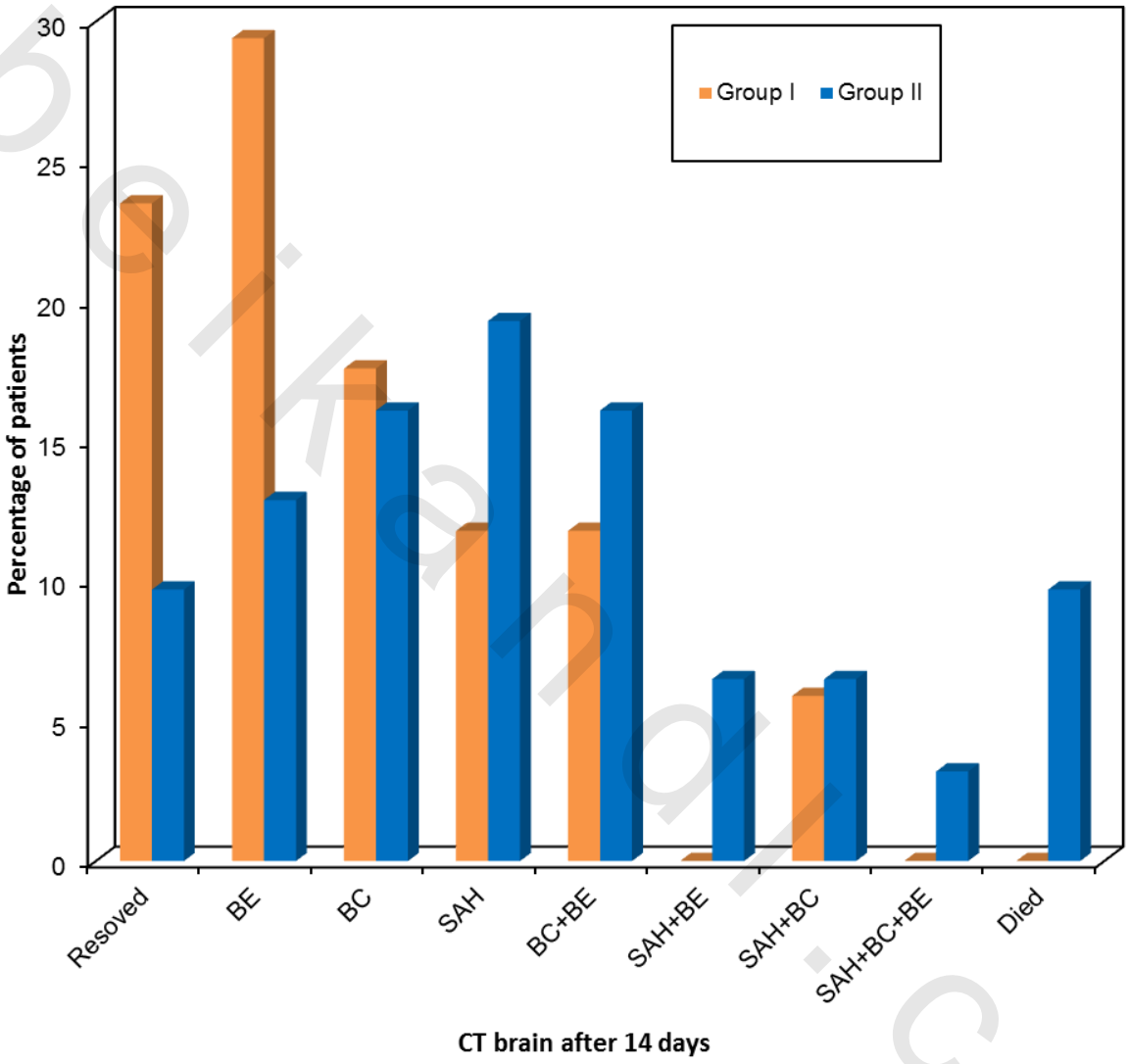


**Figure (8):** Comparison between the two studied groups according to CT Brain at the end of the study (day 14), BC, brain contusion; BE, brain edema; SAH, subarachnoid hemorrhage.

## Glasgow Coma Score (GCS) on admission Table (7) Figure (9):

The mean GCS on admission in group I was 7.47 ± 0.80, while in group II was 6.26 ± 1.32. There was statistically significant difference between the two groups according to GCS on admission ($p<0.001$), the mean GCS on admission was higher in group I than group II.

**Table (7): Comparison between the two studied groups according to GCS on admission**

| GCS on admission | Group I | Group II | P |
|---|---|---|---|
| **Admission** | **(n = 17)** | **(n = 31)** | |
| Min. - Max. | 6.0 - 8.0 | 3.0 - 8.0 | |
| Mean ± SD | 7.47 ± 0.80 | 6.26 ± 1.32 | <0.001* |
| Median | 8.0 | 7.0 | |

P, p value for Student t-test for comparing between unfavorable and favorable **;** *, Statistically significant at $p \leq 0.05$; Min, minimum, Max; maximum, SD, standard deviations.

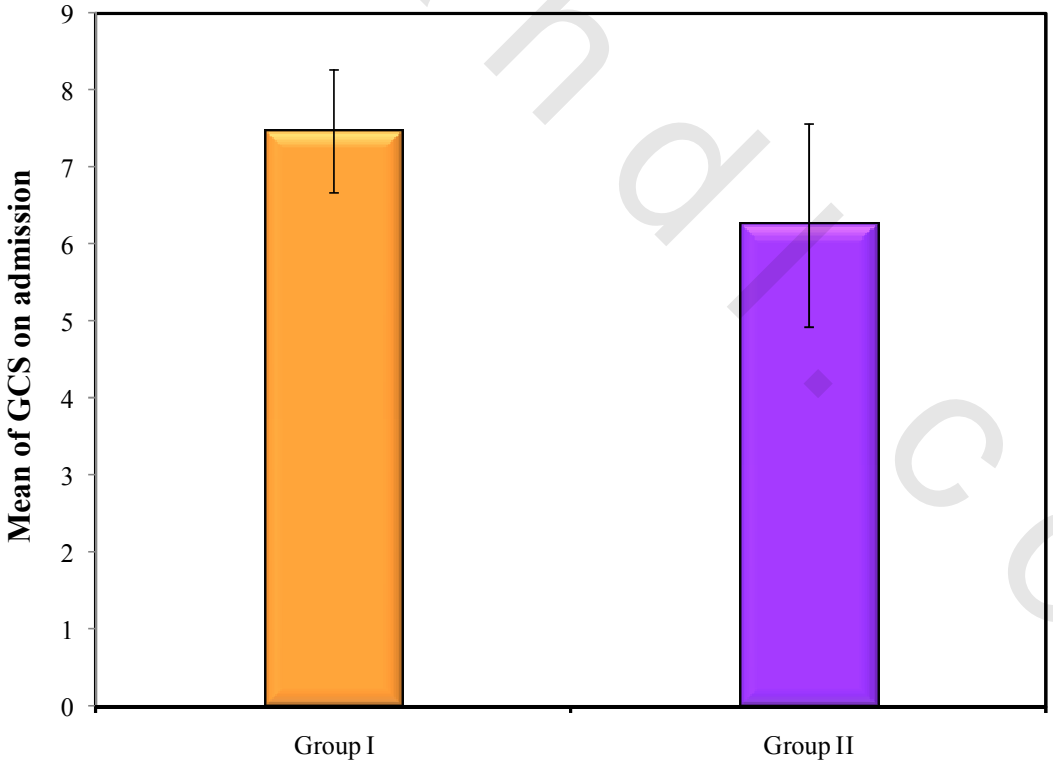


**Figure (9):** Comparison between the two studied groups according to mean GCS on admission.

## Glasgow Coma Score (GCS) at end of study (day 14) Table (8) Figure (10):

The mean GCS at end of study (day 14) in group I was 12.94 ± 1.03, while in group II was 10.10 ± 1.18. There was a statistically significant difference between the two groups according to GCS at end of study ($p<0.001$), the mean GCS at end of study (day 14) was higher in group I than group II.

**Table (8): Comparison between the two studied groups according to GCS at end of study (day 14)**

| GCS at end of study (day 14) | Group I | Group II | P |
|---|---|---|---|
| **After 14 days** | **(n = 17)** | **(n = 28)** | |
| Min. - Max. | 11.0 - 15.0 | 7.0 - 12.0 | |
| Mean ± SD | 12.94 ± 1.03 | 10.10 ± 1.18 | <0.001* |
| Median | 13.0 | 10.0 | |

P, p value for Student t-test for comparing between unfavorable and favorable **;***, Statistically significant at p ≤ 0.05; Min, minimum, Max; maximum, SD, standard deviations.

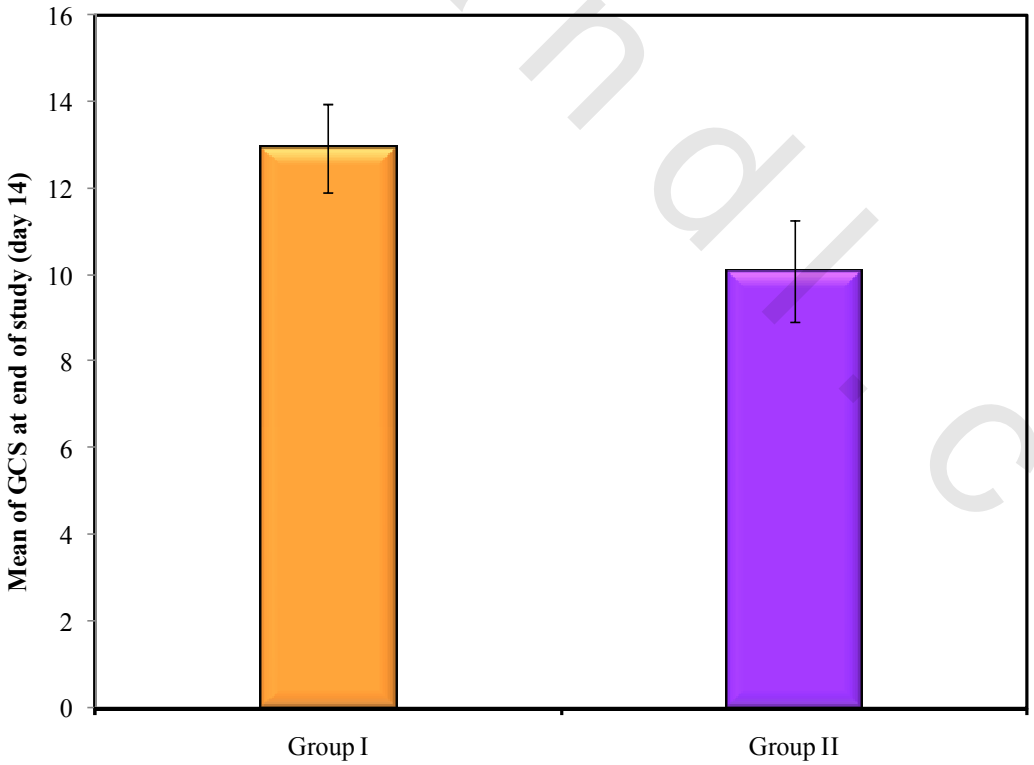


**Figure (10):** Comparison between the two studied groups according to mean of GCS at end of study (day 14).

## Glasgow Outcome Score (GOS) Table (9) Figure (11)

The mean GOS in group I was 4.24 ± 0.44, while in group II was 2.71 ± 0.64. There was a statistically significant difference between the two groups according to GOS ($p<0.001$), the mean GOS was higher in group I than group II.

**Table (9): Comparison between the two studied groups according to GOS**

| | Group I (n = 17) | | Group II (n = 31) | |
|---|---|---|---|---|
| | **No** | **%** | **No** | **%** |
| **GOS** | | | | |
| 1 | 0 | 0.0 | 3 | 9.7 |
| 2 | 0 | 0.0 | 3 | 9.7 |
| 3 | 0 | 0.0 | 25 | 80.6 |
| 4 | 13 | 76.5 | 0 | 0.0 |
| 5 | 4 | 23.5 | 0 | 0.0 |
| Min. - Max. | 4.0 - 5.0 | | 1.0 - 3.0 | |
| Mean ± SD | 4.24 ± 0.44 | | 2.71 ± 0.64 | |
| Median | 4.0 | | 3.0 | |
| **P** | <0.001* | | | |

P, p value for Mann Whitney test for comparing between unfavorable and favorable **;** *, Statistically significant at $p \leq 0.05$; Min, minimum, Max; maximum, SD, standard deviations.

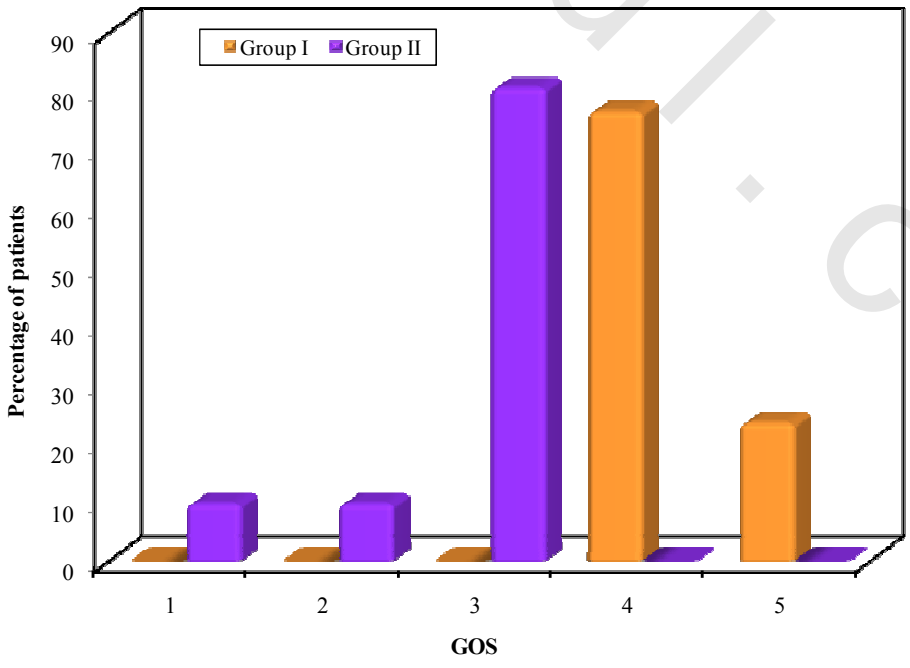


**Figure (11):** Comparison between the two studied groups according to GOS.

## Resistin level on admission Table (10), Figure (12)

The mean plasma resistin level on admission in group I was 37.92 ± 11.02 ng/ml, while it was 54.15 ± 21.16 ng/ml in group II. There was a statistically significant difference between the two groups according to plasma resistin level on admission (p=0.002). It was obviously seen that the Mean plasma resistin level was higher in group II than group I on admission.

**Table (10): Comparison between the two studied groups according to Resistin level on admission**

| Resistin level (ng/ml) on admission | Group I | Group II | P |
|---|---|---|---|
| **1st day** | **(n = 17)** | **(n = 31)** | |
| Min. - Max. | 25.38 - 67.50 | 30.0 - 97.50 | |
| Mean ± SD | 37.92 ± 11.02 | 54.15 ± 21.16 | 0.002* |
| Median | 35.0 | 43.75 | |

P, p value for Mann Whitney test for comparing between unfavorable and favorable **;** *, Statistically significant at p ≤ 0.05; Min, minimum, Max; maximum, SD, standard deviations.

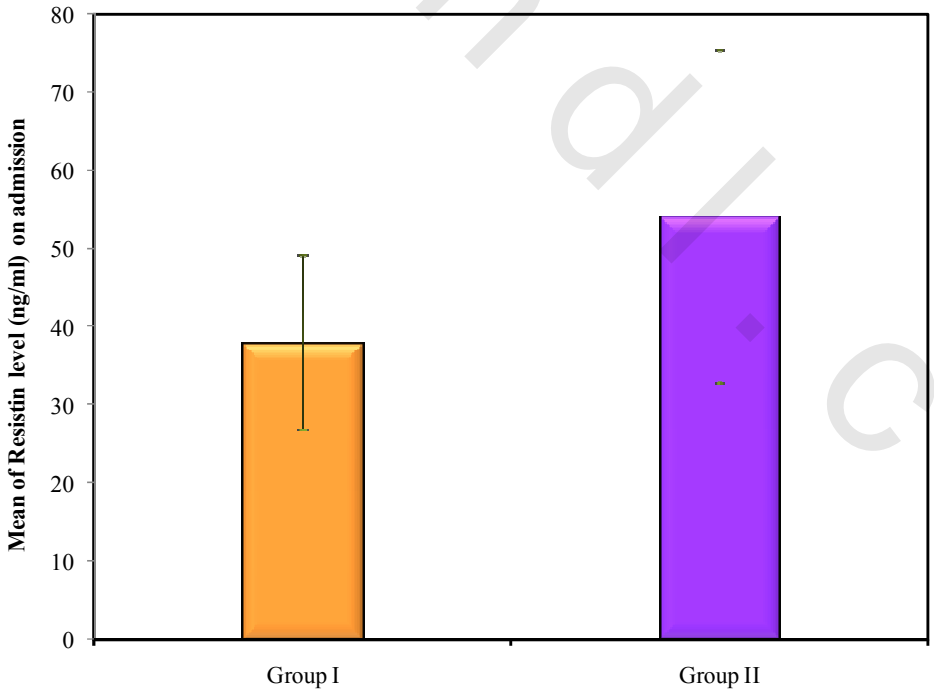


**Figure (12):** Comparison between the two studied groups according to mean Resistin level on admission.

## Resistin level on 3rd day Table (11), Figure (13)

The Mean plasma resistin level on 3rd day in group I was 21.26 ± 4.28 ng/ml, while it was 32.52 ± 8.87 ng/ml in group II. There was a statistically significant difference between the two groups according to plasma resistin level on 3rd day ($p<0.01$). It was obviously seen that the Mean plasma resistin level was higher in group II than group I on 3rd day.

**Table (11): Comparison between the two studied groups according to resistin level on 3rd day**

| Resistin level (ng/ml) on 3rd day | Group I | Group II | P |
|---|---|---|---|
| | (n = 17) | (n = 29) | |
| Min. - Max. | 14.50 - 28.75 | 25.0 - 66.25 | |
| Mean ± SD | 21.26 ± 4.28 | 32.52 ± 8.87 | <0.001* |
| Median | 20.88 | 30.0 | |

P, p value for Mann Whitney test for comparing between unfavorable and favorable **;** *, Statistically significant at $p \leq 0.05$**;** Min, minimum, Max; maximum, SD, standard deviations.

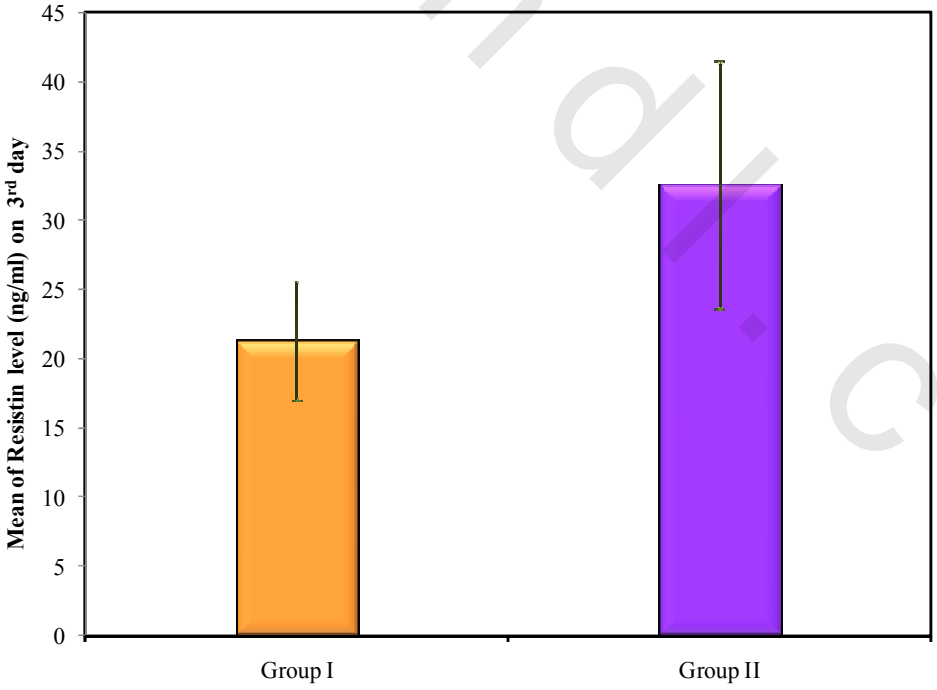


**Figure (13):** Comparison between the two studied groups according to mean of resistin level on 3rd day.

## Comparison between resistin level on admission and on third day in the two studied groups table (12) figure (14)

The mean plasma resistin level on admission in group I was 37.92 ± 11.02 ng/ml, it decreased on 3rd day to 21.26 ± 4.28 ng/ml. In group II the mean plasma resistin level decreased from 54.15 ± 21.16 ng/ml on admission to 32.52 ± 8.87 ng/ml on 3rd day.

There was a statistically significant decrease of the mean plasma resistin level on 3rd day than on admission in both groups (p<0.001).

**Table (12): Comparison between resistin level on admission and on third day in the two studied groups**

| Resistin level (ng/ml) on admission | Group I | Group II |
|---|---|---|
| **1st day** | **(n = 17)** | **(n = 31)** |
| Min. - Max. | 25.38 - 67.50 | 30.0 - 97.50 |
| Mean ± SD | 37.92 ± 11.02 | 54.15 ± 21.16 |
| Median | 35.0 | 43.75 |
| **3rd day** | | |
| Min. - Max. | 14.50 - 28.75 | 25.0 - 66.25 |
| Mean ± SD | 21.26 ± 4.28 | 32.52 ± 8.87 |
| Median | 20.88 | 30.0 |
| **p** | <0.001* | <0.001* |

P, p value for Mann Whitney test for comparing between unfavorable and favorable **;** *, Statistically significant at p ≤ 0.05**;** Min, minimum, Max; maximum, SD, standard deviations.

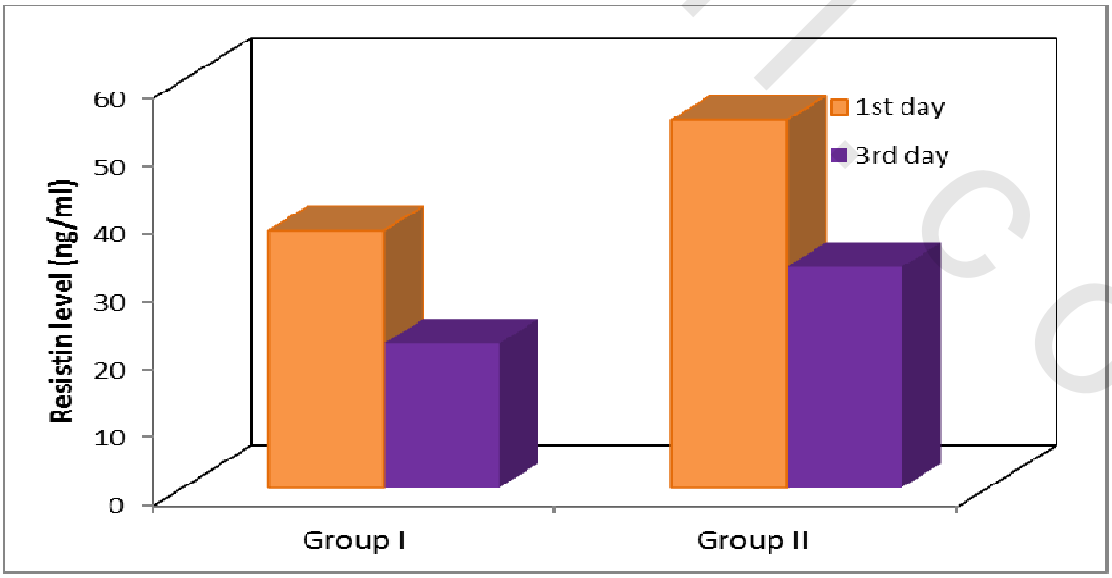


**Figure (14)**: Comparison between resistin level on admission and on third day in the two studied groups.

## Correlation between GCS and resistin level Table (13) Figure (15)

There was significant inverse correlation between the resistin level on 1st day, 3rd day and GCS (p<0.001), as resistin level increased GCS decreased.

**Table (13): Correlation between GCS and resistin level**

| | GCS | |
|---|---|---|
| | $r_s$ | p |
| **Resistin level** | | |
| 1st day | -0.894* | <0.001 |
| 3rd day | -0.781* | <0.001 |

$r_s$, Spearman coefficient; *, Statistically significant at $p \leq 0.05$.

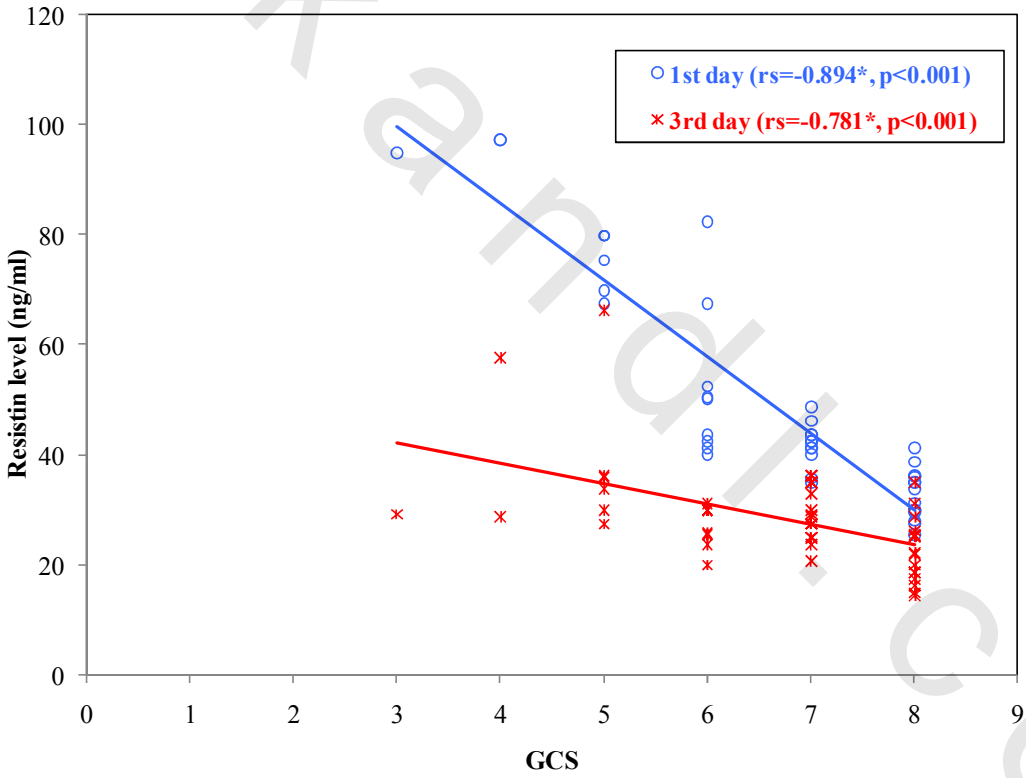


**Figure (15): Correlation between GCS and resistin level.**

## Correlation between GOS and resistin level Table (14) Figure (16)

There was significant inverse correlation between the resistin level on 1st day, 3rd day and GOS (p<0.001), as resistin level increased GOS decreased.

**Table (14): Correlation between GOS and resistin level**

| | GOS | |
|---|---|---|
| | $r_s$ | P |
| **Resistin level** | | |
| 1st day | -0.522* | <0.001 |
| 3rd day | -0.768* | <0.001 |

$r_s$, Spearman coefficient; *, Statistically significant at p ≤ 0.05.

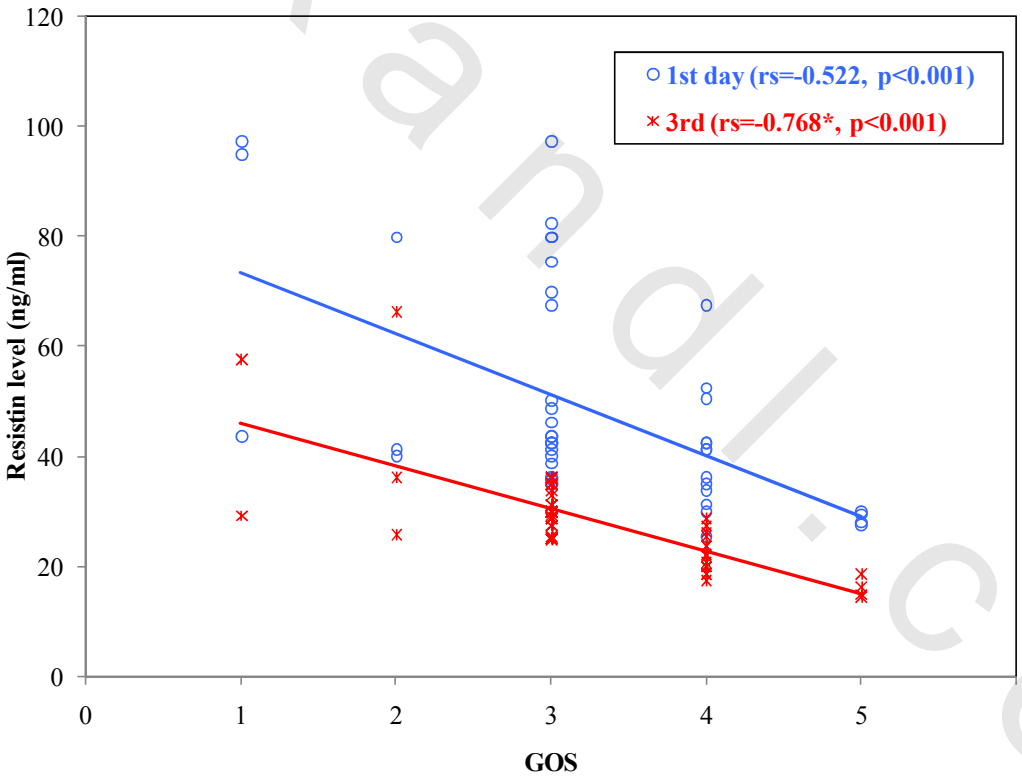


**Figure (16):** Correlation between GOS and Resistin level.

## Receiver operating characteristic (ROC) curve for resistin level Table (15) Figure (17)

Receiver operating characteristic (ROC) curves were used to describe the prognostic values of resitin, we found that The AUCs (Areas Under the Curve) for resistin on admission calculated from the ROC curves were 0.862 ($p<0.001$) . (Table15, Fig. 17)

The best prognostic cutoff point for resistin on admission was 31 ng/ml: at this level, sensitivity and specificity were 90.32 percent and 83.59percent, respectively.

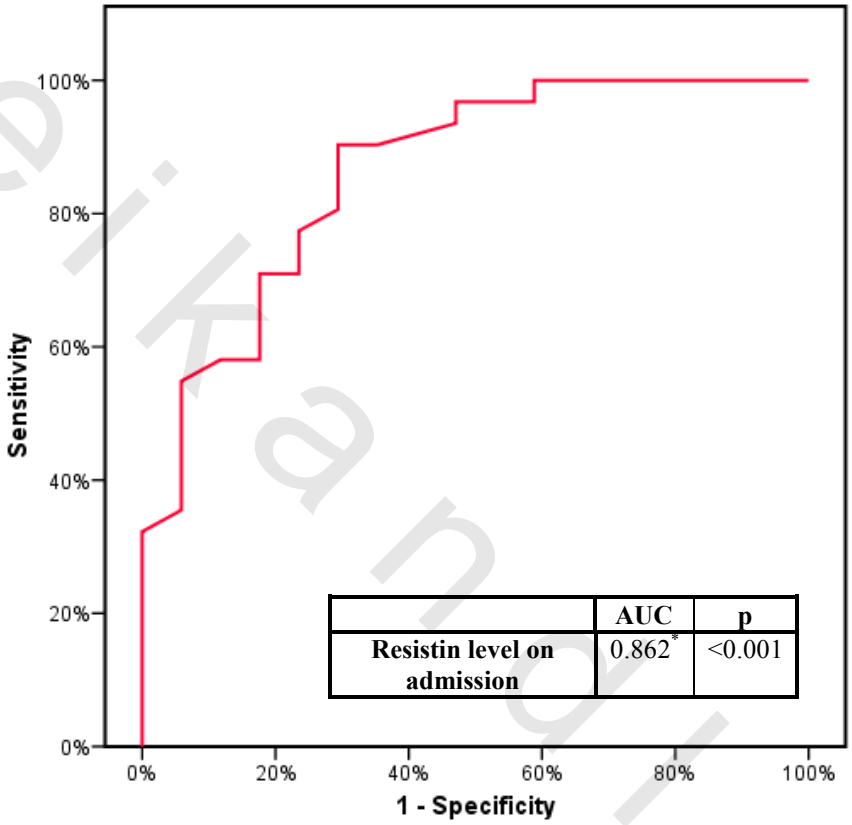


**Figure (17): ROC curve for resistin level on admission (ng/ml)**

**Table (15): Agreement (sensitivity, specificity and accuracy) of resistin level with outcome**

| | | Group I | Group II | Sensitivity | Specificity | PPV | NPV | Accuracy |
|---|---|---|---|---|---|---|---|---|
| Resistin level(ng/ml) | ≤31 | 12 | 3 | 90.32 | 83.59 | 94.85 | 80.0 | 87.33 |
| | >31 | 5 | 28 | | | | | |

PPV, positive predictive value; NPV, negative predictive value.