SUMMARY AND CONCLUSION

Leukemias are a group of disorders characterized by the accumulation of abnormal while cells in the bone marrow. These abnormal cells may cause bone marrow failure, a raised circulating white cell count and infiltrate organ.

Acute lymphoblastic leukemia is the most common form of child hood cancer. They account for about one third of new cases of cancer diagnosed each year.

The cause of leukemia is unknown in the majority of patients several factors, however, associated with the development of leukemia. These factors are environmental factor, genetic factor, viral infection and immunodeficiency.

The definitive diagnosis of leukemia is made by examination of bone marrow aspirate. Wright-Giemsa and special histochemical stains of the aspirate provide a clear diagnosis in most patients.

Certain clinical and laboratory features exhibited at diagnosis of patient with acute leukemia have prognostic value. The identification of prognostic factors has become an essential element in the design and analysis of current therapeutic trails.

Apoptosis is a form of physiological cell death, which is extremely common in many cell type and is essential for mainting stable cell

population by ensuring that the rate of new cell production is balanced by an equal rate of cell death.

In order for neoplastic cells to expand their population and subsequently form leukemia, they must escape surveillance by the host defence system. A major mechanism of such escape from growth control, at least in lymphoid cells is though to be mediated via apoptosis triggered by Fas receptor (CD95/APO-1).

CD95 is a member of tumor necrosis factor/nerve growth factor (TNF/ NGF) receptor superfamily of cell surface molecules which mediates apoptosis.

The goal of therapy in children with leukemia is to achieve along term remission while maintaining quality of life. Intensification of therapy along with improved supportive care has gradually improved the prognosis for children with leukemia.

Most of the cytotoxic drugs used in leukaemia therapy damage the capacity of cells reproduction. Combination of at least three drugs are now usually used initially to increase the cytotoxic effect improve remission rates and reduce the frequency of emergence of drug resistance. Most anticancer drugs have been shown to induce apoptosis in chemosenstive leukaemias and solid tumors.

In the present study we measured the serum level of soluble (Fas/APO-1/ CD95) in infant and children with acute lymphoblastic leukemia at presentation, 1 day after the start of induction therapy and after end of induction therapy and correlated its level with various

clinical, hematological and immunophenotyping prognostic parameters aiming at assessing its value in diagnosis and prognosis of ALL.

This study was conducted on 30 patients with acute lymphoblastic leukemia, as well as 10 healthy children age-matched as control groups.

The study included 3 steps:

(a) Pretreatment evaluation : it includes:

- Complete history and physical examination.
- Radiological examination:
  - Plain chest x-ray
  - Abdominal ultrasonography
- Laboratory investigation:
  - Complete blood count and special attention to the initial leucocytic count, platelets count, hemoglobin levels and blast cell percentage in peripheral blood.
  - Bone marrow aspiration and examination.
  - IPT to detect phenotype of the blasts cells.
  - Measurement of sFas (CD95/APO-1) in the serum of the patients by ELISA technique.

(b) 1 day after start of chemotherapy:

- Complete physical examination.
- Complete blood count.
- Measurement of sFas (CD95/APO-1) in the serum of the patients.

(c) 4 week later on:

- Complete physical examination.
- Complete blood count.
- Bone marrow aspiration and examination.
- Measurement of sFas (CD95/APO-1) in the serum of the patients.

Results of the present study showed that :

Mean of serum sFas level in patients with ALL at presentation were (7.79 ± 0.74 ng/dl) and in control children's were (1.62 ± 0.12 ng/dl) the difference was highly significant (P <0.001).

On measuring serum sFas level in all patients one day after the start of induction therapy, we found that there was no significance different between the mean of serum sFas level before and one day after the start of induction therapy (P > 0.05). The mean serum sFas levels were (7.79 ± 10.74 ng/dl) and (6.69 ± 0.70 ng/dl) respectively.

Measuring serum sFas level in patients after complete induction therapy, we found significant decrease in mean serum sFas levels after end of induction therapy than before the start of treatment (P <0.001). The mean serum sFas levels were (2.756 ± 0.53 ng/dl) and (7.79 ± 0.74 ng/dl) respectively.

By dividing the patients into two groups according to prognostic factors (high risk and low risk groups). It was found that there was significant increase in serum sFas level in high risk group than low risk group regarding age , TLC, LDH, with (P < 0.05) and IPT with (P < 0.001).

There was no significant difference in serum sFas level in high risk group than risk group regarding to sex, platelets count, haemoglobin level, organomgaly and FAB classification with (P > 0.05).

Correlation studies revealed that there were significant correlations between serum sFas levels and TLC (r = 0.728 and P <0.05) IPT (r = 0.632 and P < 0.05) and LDH (r = 0.770 and P < 0.05). There were no significant correlations between serum sFas level and other prognostic

factors (age, sex, organomegaly, hemoglobin level, platelets count, FAB classification and blast cell count.

After one month from the start of induction therapy we found that 26 cases (86.6%) achieved complete remission, two patients (6.7%) died, another two patients, (6.7%) were resistant to induction therapy.

In the 2 patients who were resistant to induction therapy, the mean serum sFas level remained high (12.7 ng/dl).

From the above result we can conclud that, sFas can be considered as diagnostic serological marker as its level was high in all cases of ALL at presentation, but not a sensitive marker after 24 hours of induction therapy as its mean level did not change from that before the start of therapy.

sFas level could serve as putative marker for active resistant leukemia as its mean level remained high in patients who were resistant to induction therapy and returned to normal level in the patients who give good response to induction therapy.

sFas level can be used as a dependant risk factor for prognosis, as there were positive correlations with some of the most important prognostic factors of ALL in children (IPT, TLC, LDH).