Expression of CD133 in acute leukemia

Fetnat M. Tolba · Mona E. Foda · Howyda M. kamal · Deena A. Elshabrawy

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Abstract There have been conflicting results regarding a correlation between CD133 expression and disease outcome. To assess CD133 expression in patients with acute myeloid leukemia (AML) and acute lymphoblastic leukemia (ALL) and to evaluate its correlation with the different clinical and laboratory data as well as its relation to disease outcome, the present study included 60 newly diagnosed acute leukemic patients; 30 ALL patients with a male to female ratio of 1.5:1 and their ages ranged from 9 months to 48 years, and 30 AML patients with a male to female ratio of 1:1 and their ages ranged from 17 to 66 years. Flow cytometric assessment of CD133 expression was performed on blast cells. In ALL, no correlations were elicited between CD133 expression and some monoclonal antibodies, but in AML group, there was a significant positive correlation between CD133 and HLA-DR, CD3, CD7 and TDT, CD13 and CD34. In ALL group, patients with negative CD133 expression achieved complete remission more than patients with positive CD133 expression. In AML group, there was no statistically significant association found between positive CD133 expression and treatment outcome. The Kaplan–Meier curve illustrated a high significant negative correlation between CD133 expression and the overall survival of the AML patients. CD133 expression is an independent prognostic factor in acute leukemia, especially ALL patients and its expression could characterize a group of acute leukemic patients with higher resistance to standard chemotherapy and relapse. CD133 expression was highly associated with poor prognosis in acute leukemic patients.

Keywords CD133 · AML · ALL · Flow cytometry

Introduction

Although outcome for children with pediatric acute lymphoblastic leukemia (ALL) has improved considerably in recent years, a significant proportion of cases relapse [1]. The complexity of the leukemogenic process, together with our limited understanding of the biology of this disease, presents a challenge to developing novel therapeutic approaches [2].

Developments in flow cytometric techniques and the availability of lineage-associated monoclonal antibodies have permitted characterization of normal and leukemic cells and affirmed the immunophenotypic heterogeneity in ALL [3]. Evidence suggests that ALL has a primitive cell origin and shares many immunophenotypic characteristics with normal progenitor cells. These leukemic stem cells may be resistant to current therapeutic strategies, and subsequent relapses may arise from this population [4]. These cancer stem cells have been shown to express CD133 (AC133), a primitive cell antigen [1], that has been shown to be more specific marker of hematopoietic stem cells than CD34 [5].

There have been conflicting reports on the expression of CD133 in ALL, whereas some found high levels of CD133 expression on particular cases [6]. Others detected only few levels [7] or none at all [8]. The current classification of acute myeloid leukemia (AML) is based predominantly on the cytogenetic abnormalities and morphology of malignant blasts but it is not always helpful for optimization of the treatment strategy [9].
Human CD133 (AC133) is a novel five-transmembrane molecule, which is expressed on primitive normal hematopoietic progenitor. AC133 reacts with a population of non-committed or granulomonocytic GM-committed CD34+ cells in normal hematopoiesis. CD133 reactivity was observed in cases of AML, especially myelomonocytic different AML FAB M4/M5 cases [10].

In the hematopoietic system, CD133 is expressed on a subset 30–70 % of the CD34+ cells in the human bone marrow, fetal liver, umbilical cord blood and growth factor primed peripheral blood [11]. The expression of CD133 on primitive AML cells is unknown, while it has been reported that CD133 is expressed on the majority of bulk CD34+ AML cells, whereas CD133 expression on CD34− AML cells is low to absent in most but not all cases [12].

**Aim of the work**

The aim of this work is to assess CD133 expression in patients with acute myeloid or lymphoblastic leukemia and to evaluate its correlation with the different clinical and laboratory data as well as its relation to disease outcome.

**Patients and methods**

The present study included 60 subjects, selected from Benha University Hospital. They were divided into two groups: The first group (ALL) included 30 newly diagnosed patients with acute lymphoblastic leukemia. They were (18) males and (12) females with a male to female ratio of 1.5:1 and their ages ranged from 9 months to 48 years. The second group (AML) included thirty (30) newly diagnosed AML patients. They were 15 males and 15 females with a male to female ratio of 1:1 and their ages ranged from 17 to 66 years.

All patients were subjected to the following: Detailed history: with special emphasis on age, sex, presence of leukemia associated symptoms (fever, easy fatigability, bleeding tendency and bone aches). Thorough clinical examination: laying stress on the presence and extent of leukemia involvement including: pallor, purpuric eruptions, size of liver and spleen and lymphadenopathy. Laboratory investigations: complete blood count (CBC) using Sysmex kx-21, with examination of Leishman-stained PB smears for differential leukocytes count and blast cells percentage. BM aspiration and examination of Leishman stained smears to detect the percentage of BM blast cells. Cytochemical study for blast cells by myeloperoxidase was performed on the marrow smears. The diagnosis of acute leukemia was based on the morphological criteria established by the FAB group as well as myeloperoxidase and the immunophenotypic pattern results consistent with AML and ALL. Immunophenotyping of blast cells in BM aspirates samples using FACSCalibur Flow Cytometer (Becton Dickinson (BD) USA), was done to determine percentage of blast cells expressing CD133. AML patients received the standard “3 + 7” induction chemotherapy protocol: doxorubicin (30 mg/m2/day) for 3 days and cytarabine (100 mg/m2/day as a continuous 24-h intravenous infusion) for 7 days [13]. BMA was done between 21 and 28 days after initiation of chemotherapy to demonstrate morphological remission. Consolidation is comprised of three to four courses of high-dose cytosine arabinoside (3 g/m2 every 12 h on days 1, 3 and 5; total, 18 g/m2). Patients were followed up once every 3 months with clinical examination and complete blood counts. BMA was done if there was any doubt of a relapse on clinical examination or peripheral smear. The induction chemotherapy regimens of ALL patients were as follows: vincristine 1.5 mg/kg/m3/week IV (days 0, 7, 14, 21, 28, 35), doxorubicin 25 mg/m3/week IV infusion (days 0, 7, 14, 21, 28, 35), L-asparaginase 6000 u/m3 SC on alternate days for 10 doses, and prednisone 40 mg/m3/day for 6 weeks orally. On day 21, bone marrow aspiration was done. In non-responding cases, we add etoposide 100 mg/m3/dose IV (days 22, 25, 39), cyclophosphamide 750 mg/m3/dose IV infusion (days 22, 25, 29), aracytine 100/m3/dose IV (days 22, 25, 29), and high-dose methotrexate 6 g/mm3 over 4 h on day 8.

Assessment of remission achievement was done after the induction of therapy by BM on day 14 and day 28, as well as by CBC evaluation and follow-up of the patients throughout the period of the study. Monoclonal antibodies (MoAbs) supplied by Becton/Dickinson Biosciences (BDB; San Jose, CA) were used. The panel of fluorescein isothiocyanate (FITC)/phycoerythrin (PE)/peridinin chlorophyll protein (PerCP)-conjugated MoAbs was used for each sample to be diagnosed as AML and ALL includes: myeloid markers: CD13, CD33, intracellular MPO, monocytic marker: CD14, CD64, lymphoid markers: TDT, B cell markers: CD19, CD20, CD10, CD22, CD79a, T cell markers: CD3, CD5, CD7, common progenitor marker: CD34, HLA-DR and PE labeled MoAb for detection of CD133 (Miltenyi Biotec, Germany). BM samples were processed within 24 h of collection at room temperature. A minimum of 10,000 events were studied. Gating was done on the blast cell population based on forward and side scatter properties. The percentage of blast cells positive for the relevant studied marker was determined as a percentage from the gated blast cells population. Cells were considered positive for a certain marker when ≥20 % of cells expressed it, except for CD34, TDT, CD133 and intracellular MPO where its expression by 10 % of cells was sufficient to confer positivity. The negative isotypic control was set at 5 %.
Statistical analysis

The collected data were tabulated and analyzed using statistical package of social science (SPSS) version 17 software. Suitable statistical techniques were computed “ANOVA” test, Mann–Whitney “U” test, Student’s “t” test, “Z” test and Spearman’s correlation coefficient were used as tests of significance. Qualitative data were described in the form of number and percentage. Quantitative data were described in the form of mean ± standard deviation (SD), range and median.

Results

In ALL group, there were (18) males and (12) females with a male to female ratio of 1.5:1 and their ages ranged from 9 months to 48 years with the mean 15.8 ± 12.4, while in AML group, they were ranged from 17 to 66 years, with a mean age of 34.3 ± 15.2 years. They were 15 males and 15 females with a male to female ratio of 1:1. Clinical and demographic data of ALL and AML groups represented in Table 1.

There was no significant association elicited between CD133-positive expression and any of the studied demographic and clinical parameters of patients in ALL and AML groups (Table 2). Regarding correlations between CD133 expression and some of the studied standard prognostic factors concerning the age and other laboratory data in ALL and AML groups, no statistically significant difference was elicited (Table 3) except for a significant correlations between CD133 expression and TLC among ALL patients ($p < 0.01$).

As regarding correlations between CD133 expression and some monoclonal antibodies, in ALL, no correlations were elicited, but in AML group, there were significant correlations between CD133 and HLA-DR, CD3, CD7 and TDT ($p < 0.05$), high significance for CD13 ($p < 0.01$) and very high significance for CD34 ($p < 0.001$) (Table 4).

In ALL group, 22/30 (73.3 %) patients showed good response to chemotherapy and achieved complete remission till the end of follow-up period (1 year), 2/30 patient (6.7 %) died and 6/30 (20 %) patients developed resistance to chemotherapy. On the other hand, in AML group, 19/30 (63.3 %) patients showed good response to chemotherapy and achieved complete remission till the end of follow-up period (12 months), 6/30(20 %) patients died and 5/30 (16.7 %) patients developed resistance to chemotherapy (Table 5). Also, there was no statistically significant association found between positive CD133 expression and treatment outcome in AML patients ($p > 0.05$). Despite the absence of significance, there is an increasing CD133 mean among the cases with chemotherapeutic resistance. The Kaplan–Meier curve (Fig. 1) and the data in (Table 6) illustrated the high significance correlation between CD133 expression and the overall survival of the AML patients indicating that increasing CD133 leads to decrease the survival by the time. On the other hand, there was a significant difference between CD133 expression and clinical outcome among ALL patients. In addition, there was a significant difference between remission group with positive CD133 and remission group with negative CD133 (Z test = 2.04), and a significant difference between resistant group with

<table>
<thead>
<tr>
<th>Variable</th>
<th>Group I (ALL)</th>
<th>Group II (AML)</th>
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<tbody>
<tr>
<td>Age (mean ± SD)</td>
<td>15.8 ± 12.4</td>
<td>34.3 ± 15.2</td>
</tr>
<tr>
<td>Gender (male), no, %</td>
<td>18 (60.0 %)</td>
<td>15 (50.0 %)</td>
</tr>
<tr>
<td>Pallor</td>
<td>24 (80.0 %)</td>
<td>13 (43.3 %)</td>
</tr>
<tr>
<td>Fever</td>
<td>22 (73.3 %)</td>
<td>19 (63.3 %)</td>
</tr>
<tr>
<td>Bleeding tendency</td>
<td>8 (26.7 %)</td>
<td>8 (26.7 %)</td>
</tr>
<tr>
<td>Lymph node</td>
<td>22 (73.3 %)</td>
<td>5 (16.7 %)</td>
</tr>
<tr>
<td>Hepatosplenomegaly</td>
<td>17 (56.7 %)</td>
<td>23 (76.7 %)</td>
</tr>
<tr>
<td>CNS manifestations</td>
<td>0 (0.0 %)</td>
<td>2 (6.7 %)</td>
</tr>
<tr>
<td>Mediastinal mass</td>
<td>6 (20.0 %)</td>
<td>2 (6.7 %)</td>
</tr>
<tr>
<td>Bone pain</td>
<td>20 (66.7 %)</td>
<td>13 (43.4 %)</td>
</tr>
</tbody>
</table>

There was no significant association elicited between CD133-positive expression and any of the studied demographic and clinical parameters of patients in ALL and AML groups (Table 2). Regarding correlations between CD133 expression and some of the studied standard prognostic factors concerning the age and other laboratory data in ALL and AML groups, no statistically significant difference was elicited (Table 3) except for a significant correlations between CD133 expression and TLC among ALL patients ($p < 0.01$).

As regarding correlations between CD133 expression and some monoclonal antibodies, in ALL, no correlations were elicited, but in AML group, there were significant correlations between CD133 and HLA-DR, CD3, CD7 and TDT ($p < 0.05$), high significance for CD13 ($p < 0.01$) and very high significance for CD34 ($p < 0.001$) (Table 4).

In ALL group, 22/30 (73.3 %) patients showed good response to chemotherapy and achieved complete remission till the end of follow-up period (1 year), 2/30 patient (6.7 %) died and 6/30 (20 %) patients developed resistance to chemotherapy. On the other hand, in AML group, 19/30 (63.3 %) patients showed good response to chemotherapy and achieved complete remission till the end of follow-up period (12 months), 6/30(20 %) patients died and 5/30 (16.7 %) patients developed resistance to chemotherapy (Table 5). Also, there was no statistically significant association found between positive CD133 expression and treatment outcome in AML patients ($p > 0.05$). Despite the absence of significance, there is an increasing CD133 mean among the cases with chemotherapeutic resistance. The Kaplan–Meier curve (Fig. 1) and the data in (Table 6) illustrated the high significance correlation between CD133 expression and the overall survival of the AML patients indicating that increasing CD133 leads to decrease the survival by the time. On the other hand, there was a significant difference between CD133 expression and clinical outcome among ALL patients. In addition, there was a significant difference between remission group with positive CD133 and remission group with negative CD133 (Z test = 2.04), and a significant difference between resistant group with

<table>
<thead>
<tr>
<th>Variable</th>
<th>Group I (ALL)</th>
<th>Group II (AML)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male gender</td>
<td>8 (80.0 %)</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Pallor</td>
<td>8 (80.0 %)</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Fever</td>
<td>8 (80.0 %)</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Bleeding tendency</td>
<td>1 (1.0 %)</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Lymph nodes</td>
<td>7 (70.0 %)</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>CNS manifestations</td>
<td>0 (0.0 %)</td>
<td>–</td>
</tr>
<tr>
<td>Mediastinal mass</td>
<td>2 (20.0 %)</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Bone pain</td>
<td>8 (80.0 %)</td>
<td>&gt;0.05</td>
</tr>
</tbody>
</table>

* $p < 0.05$ (significant)
positive CD133 and resistant group with negative CD133 (Z test = 1.94) and no significant difference between dead group with positive CD133 and dead group with negative CD133 (Z test = 0.52) (Table 6).

**Discussion**

Leukemia arises through the acquisition of genetic mutations in hematopoietic stem or progenitor cells, resulting in impairment of hematopoietic and unrestrained proliferation of an immature clone. The condition is lethal within a few months without treatment, but most young patients reach complete remission with chemotherapy. Many of them will relapse after a while, but an increasing number of young people survive for a long time [14].

It has been assumed that in most cases, the leukemic cells reflect the immunophenotype of normal hematopoietic cells of either myeloid or lymphoid lineage blocked at various stages of differentiation, defined both by antigens expressed and the absence of expression of antigens associated with a different lineage or certain stages of maturation. Usually, CD34 and HLA-DR used for the myeloid or TdT used for the lymphoid leukemia has been useful to distinguish between immature cells [15].

Given the fact that CD133 antigen is expressed restrictively in the more immature subset of the CD34 + cell population, we could expect the CD133 antigen to be more valuable prognostic marker compared to the CD34 antigen. It has also been suggested that, like the CD34 antigen, expression of the CD133 antigen in acute leukemia could be correlated with either a more immature phenotype of the blast population or to a bad prognosis [8].
Assessment of the prognosis of acute leukemia involves a number of clinical and laboratory criteria such as morphology, surface markers, cytogenetics and other recent criteria such as transcription factors and cytokines. Immunophenotypical studies of acute leukemia patients have shown that the CD34 antigen is expressed in a relatively high proportion of cases ranging from 30 to 60% in AML and from 60 to 70% in ALL, and that its presence has been related to more immature morphological and immunophenotypical features, as well as a poorer prognosis [16]. However, controversies exist in the previous literature concerning the correlation of CD34 expression and clinical outcome in acute leukemias [17]. CD133 is a marker for adult stem cells in various tissues and tumor types. Stem cell specificity is maintained by tight regulation of CD133 expression at both transcriptional and post-translational levels [18].

**ALL group**

CD133 was positive in 10/30 (33.3%) cases only of ALL patients, and the frequency of CD34 expression was proved to be found on 100% of CD133-positive cases. These groups of patients show high degree of immaturity as TDT was also 100% expressed on cases with CD133 positive. To elucidate the value of CD133 expression as a prognostic factor in acute leukemia, we investigated the significance of its expression in relation to various clinical, laboratory and standard prognostic factors, as well as to treatment response and clinical outcome of patients. No significant difference was noted between age of patients and positivity for CD133 expression. This is in concordance with Horn et al. [8], Lee et al. [19] and Guenova and Balatzenko [15].

Lee et al. [19] found that no significant association was detected between the gender and positive CD133 expression in their study, which is in agreement with the results of the present study. In agreement with reports by Vercauteren and Sutherland [20], as well as Lee et al. [19], no association was elicited between clinical variables and CD133 expression. Different laboratory variables showed no significant associations with CD133-positive expression except TLC. These results are in similarity to those reported by Zhou et al. [21], who found no significant association between CD133 expression and any laboratory variables.

Contradictory, Wang et al. [22] detected a significant correlation between CD133 expression and CD34 expression. There was disagreement between this result and ours, as no significant correlation was found between CD133 expression and CD34 expression in this current study. This conflict between our results and the above study could be explained by the difference in the methods used in evaluating CD133 expression on acute leukemia blasts, where we used flow cytometry, and in the latter study, immunocytochemistry method was used to examine the expression of CD133 on blasts of patients with acute leukemia.

Regarding the relation between CD133 expression and various studied standard prognostic factors, no statistically significant association was found between the studied prognostic factors such as sex, age, the percentage of leukemic blast cells in PB and in BM, hemoglobin concentration, platelet counts and CD133 expression. This is consistent with the results obtained by Fauth et al. [23], Lee et al. [19], Kim [24], Zhou et al. [25], Taguchi [26] and Wang et al. [22]. We found a highly significant correlation between CD133 expression and TLC, this result is in contrast with Wang et al. [22], who found no significant correlation between TLC and CD133 expression.

To further elucidate the prognostic significance of CD133, prognosis was studied in relation to CD133 expression. Its expression was significantly related to the response of chemotherapy, where a statistically significant increase in the number of non-responders who had positive CD133 expression 4/10 (40%) was detected when compared to non-responders who had negative CD133 expression 2/17 (10%); these results are consistent with reports by Zhou et al. [21] who stated that CD133-positive

### Table 6 Correlation between CD133 and clinical outcome

<table>
<thead>
<tr>
<th>Group</th>
<th>CD133 +ve (n = 10)</th>
<th>CD133 -ve (n = 20)</th>
<th>Remission</th>
<th>Resistance</th>
<th>Dead</th>
<th>Test of significant</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>No %</td>
<td>No %</td>
<td>No %</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group I (ALL)</td>
<td></td>
<td></td>
<td>5 50.0</td>
<td>4 40.0</td>
<td>1 10.0</td>
<td>X2 = 4.4</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>(mean ± SD)</td>
<td>10.2 ± 18.9</td>
<td>40.3 ± 30.7</td>
<td>17 ± 12.4</td>
<td>F = 4.64</td>
<td>&gt;0.05&gt;0.05&gt;0.05</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group II (AML)</td>
<td></td>
<td></td>
<td>11 64.7</td>
<td>4 23.5</td>
<td>2 11.8</td>
<td>Z1 = 0.51 Z2 = 1.15 Z3 = 1.3</td>
<td>&gt;0.05&gt;0.05&gt;0.05</td>
</tr>
<tr>
<td>(mean ± SD)</td>
<td>16.5 ± 12.6</td>
<td>26.2 ± 26.5</td>
<td>11.1 ± 16.8</td>
<td>F = 1.3</td>
<td>&gt;0.05</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*p < 0.05 (significant)*
expression is an independent poor prognostic factor in childhood acute leukemia and could characterize a group of patients with resistance to standard chemotherapy, as well as high incidence of relapse and death (Elgendi et al.) [16].

To clarify the value of CD133 in determining the clinical outcome, the positivity of CD133 expression at diagnosis was compared between the patients being stratified according to their clinical outcome. Eighty-five percent (17 patients out of 20) of ALL patients who achieved complete remission were negative for CD133 expression on their blasts, while, on the contrary, 10% (1/10) of ALL cases that died by the end of the follow-up period had positive CD133 expression. Moreover, 40% (4 out of 10) of ALL cases that developed resistance to chemotherapy were positive for CD133 expression.

These results are consistent with reports by Lee et al. [19], as well as Zhou et al. [25] and Elgendi et al. [16], who found a trend toward higher CR rates in CD133-negative ALL cases when compared to CD133-positive ones. Furthermore, Horn et al. [8], as well as Elgendi et al. [16], reported a tendency for poorer outcomes in CD133-positive ALL compared to CD133-negative ones.

Crucially, Cox et al. [27] demonstrated that AC133+/CD19− ALL cells were more resistant to treatment with dexamethasone and vincristine, key components in childhood ALL therapy, than the bulk leukemia population. The observed resistance could not be attributed to disease status or initial risk stratification. Therefore, as reported by Langer et al. [28] and Cox et al. [27], the poor clinical outcomes associated with positive CD133 expression in ALL and AML cases could be explained by the fact that CD133+ cells show increased resistance to chemotherapeutic agents which in turn is attributed to the fact that there is a higher expression of the multidrug resistance gene breast cancer resistance protein 1 and DNA mismatch repair genes, as well as genes that inhibit apoptosis in the CD133-expressing cancer stem cell (CSC). Moreover, it was proved that the striking associations between expression of CD133 and antiapoptotic proteins (bcl-2 and bcl-xl) are responsible for decreased rates of CR [29].

AML group

No significant difference was noted between age of patients and the cases which were positive for CD133 expression and those negative for it. This is in concordance with a study done by Horn et al. [8] as well as another one done by Christian et al. [30], Lee et al. [19] and Guenova and Balatzenko [15].

No male predominance in AML was obviously seen in the present study (male to female ratio 1:1), with no significant association detected between the gender and positive CD133 expression. In a study done by Lee et al. [19], the male to female ratio, on 56 acute leukemia patients, was 1:1, yet no significant association was detected between the gender and CD133 expression in that study, which is in agreement with the results of the present study.

Despite the presence of lymphadenopathy, hepatomegaly and splenomegaly provides an indirect measurement of leukemic cell burden, none of these clinical variables had any significant association with positive CD133 expression in the present study but most of the patients with hepatosplenomegaly investigated with flow cytometry have stem cell marker CD133+. Also, positive CD133 showed no significant association with other clinical features as presence of fever, pallor or bleeding tendency. This is in concordance with Zhou et al. [21], who found that CD133 was not correlated with any clinical variables.

There were no significant correlations of the hematological data of the patients and CD133 in the present study. These results are in agreement with those reported by Zhou et al. [21] and Wang et al. [22], who found no significant association between CD133 expression and WBC count, PLT count, Hb percentage and the number of blast cells which present either peripherally or in the bone marrow.

The frequency of positive CD133 expression was 56.7% (17/30 cases) among AML patients. However, in a study by Lee et al. [19], the frequency of positive CD133 expression was 38.9% (14/36 cases) among AML patients. As regards CD133 relation to various standard prognostic factors, no significant association was detected between it and any of these factors as sex and various clinical variables (e.g., presence of organomegaly or lymphadenopathy). This is in agreement with Wang et al. [22], who reported that the expression of CD133 had no relationship with prognostic factors such as sex, age and various clinical variables.

There was a significant correlation between HLA-DR and CD133 (<0.05) that agreed with Zhou et al. [25]. The significance between CD133 and the lymphoid markers CD7, CD3 and TdT (<0.05) was high.

The high significant association between the myeloid marker CD13 and CD133 expression (<0.01) indicates directly proportional relationship between the two marker which may give a picture about using it as a myeloid marker in the future (CD133 and CD34 are early markers for stem cells). Wang et al. [22] in their study showed that there is a significant correlation between CD133 and CD34. This is in concordant with ours that showed CD133 expression (88.2%) with CD34+ cells. Statistically, there was high significant association between them (p < 0.001).

To further elucidate the prognostic significance of CD133 and its expression was studied in relation to treatment response in the thirty AML patients, CD133 has shown to
have no significant relation to the response to chemotherapy in despite of the increasing mean range of CD133 present with resistant cases to chemotherapy. This is in agreement with Zhou et al. [25] which stated that CD133 expression was associated with reduced response to treatment in AML. However, the number of patients screened in our study might still not be sufficient to give a conclusive answer. Although more than one study had proved the association between CD133 expression and shorter remissions and disease-free survival in AML patients, Lee et al. [19], Lichtman and Liesveld [31] and Vercauteren and Sutherland [20], studied on 92 AML patients, found that CD133 expression was not correlated with disease-free survival (DFS) or overall survival time (OST) of these patients. This difference between the studies could be due to the difference in the sensitivity of methods of assay of CD133, variability of reagents used for the assay of CD133, and therapy protocols applied for AML patients.

The unfavorable prognosis conferred by CD133 expression was consolidated by studying the OST for the 30 newly diagnosed AML patients, using Kaplan–Meier curves. We found that the increased expression of this protein was significantly associated with a shorter OST along the 12-month period of the study. However, in a study performed by Lee et al. [19], the increased expression of this protein was not significantly associated with a shorter OST.

Conclusion

CD133 expression is an independent prognostic factor in acute leukemia, especially ALL patients and its expression could characterize a group of acute leukemic patients with higher resistance to standard chemotherapy, relapse or death. CD133 expression was highly associated with poor prognosis in acute leukemic patients.

Conflict of Interest

None

References