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Research Article

ACUTE PROMYELOCYTIC LEUKEMIA 38 CASES REVIEW AND ANALYSIS FOR FIVE YEARS

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ABSTRACT

OBJECTIVES: Analysis of APL for five years, to compare the reviewed data at Dali Clinical Medical College affiliated to Dali University, their clinical course, laboratory analysis, and treatment outcome, complications after treatment, overall survival and complete remission rate of new patients and make more understanding of APL to other published researches data.

MATERIAL AND METHODS: There were 38 newly admitted cases of APL at Dali Clinical Medical College affiliated to Dali University between the January 2013 & December 2017. Retrospective -analysis to collect all clinical data done on the basis of age, gender, ethnicity, clinical features, typical laboratory investigations, bone marrow examinations, final diagnosis, treatments, complications after treatment and survival rates. Data were analyzed with SPSS version 22.

RESULTS: Among 38 cases studied, the mean age was 38 years and the median age was 39 years (p value<.581). The female to male ratio was 1.9:1 (P value<.748). Thirty-one patients (81.58%) achieved CR (P value <.001). Complication during induction therapy were Intracranial Hemorrhage in four patients (10.53%), DIC in five patients (13.16%) and Retinoic Acid Syndrome in two patients (5.26%) reported. During Induction & follow up, total of 10 (26.32%) patients died, out of which 7(18.4%) died during induction due to the socioeconomic problem, and 3(7.9%) died during maintenance therapy. Median OS is 73.7% (p value<0.22). Median disease-free survival (DFS) is 90.3% (p value=1.000)

CONCLUSIONS: With a view to reduce the gap in outcome between the developed and those in the developing countries quicker diagnosis and better supportive cares, early recognition and treatment of life-threatening complications are required. ATRA and combination chemotherapy results in high complete remission rates and low relapse rate in newly diagnosed APL. The incidence of APL is slightly higher in female populations.

Keywords: Acute Promyelocytic Leukemia, Case Review and Analysis, Survival.

INTRODUCTION

This is a subtype of Acute Myeloid Leukemia (AML) characterized by an arrest in maturation at the Promyelocytic stage, leading to inhibition of normal hematopoiesis. First defined as a distinctive entity in 1957 by Hillestad (1957). It is characterized by chromosomal translocation t (15; 17) [1]. It constitutes 15-10% of all cases of AML and is regarded as the most curable subtype of AML [2, 3]. The peak incidence of APL is in typically younger than other subtypes of AML. Disseminated Intravascular Coagulation (DIC) may occur with any subgroup of AML but it is especially more common in acute PML (M3) [3].

Acute Promyelocytic Leukemia (APL) has been previously classified as the AML-M3 category to the French-American- British (FAB) morphological classification system, [4] and then as APL with t (15; 17) (q24.1; q21.1) translocation produces a fusion gene Promyelocytic Leukemia-Retinoic Acid Receptor Alpha (PML-RARA) by World Health Organization [5, 6].

Morphologically, there are two variants of APL, most cells are hypergranular variant while micro-granular variant is accountable in 25% of cases but is more aggressive than the hyper granular type [7]. The micro-granular variant is also associated with a higher risk of early hemorrhagic death.

APL patients are segregated into low-risk (WBC count ≤ 10 × 10^9/L, platelet count > 40 × 10^9/L), intermediate-risk (WBC count ≤ 10 × 10^9/L, platelets ≤ 40 × 10^9/L), and high-risk (WBC count > 10 × 10^9/L) groups, with distinctive outcomes [8].

However, the treatment of patient with PML has been dramatically improves its prognosis and APL is now associated with the highest proportion of AML patients who are cured of their disease. In this article, I will give my personal opinions about the modern treatment like ATRA plus ATO of newly diagnosed APL is treated differently from all other subtypes of AML and has become the most curable type of AML [9, 10].

Data for APL patients from our centre is limited. We have reviewed records of the patients diagnosed at our centre during the past five years. This report describes the demographic data, clinical features, laboratory findings, treatment and risk stratification in APL patients.

This study hoped to be a benefit to the colleague's doctors to recognize APL in the early stage and treat it early for better prognosis. In Dali, Yunnan there is no research done about this topic so it will fill up the gap for local studies, for further research about APL from my findings and conduct follow up analysis and to raise awareness among the local population about APL.

MATERIALS AND METHODS

A retrospective study conducted at Dali University-affiliated hospital, Dali, xiaguan, which is an A retrospective study conducted at Dali University-affiliated hospital, Dali, xiaguan, which is an over 1500 bed in this hospital. We retrieved the data from 38 patients with confirmed diagnosis of APL presented between the calendar year January 2013 to December 2017 was done.

The Study was divided on the basis of age of detection, the presence of clinical features, hematological parameters, liver and renal function test and bone marrow studies.

Hematological parameters were determined by cell Dyne (Abbott. Diagnostics). Bone marrow aspirate and trephine biopsy were reviewed by consultant hematopathology. Conventional G-band karyotype analysis (cytogenetic) was performed on bone marrow aspirate specimens. In negative cases diagnosis was confirmed by the presence of the PML/RARα fusion gene, which was performed on interphase nuclei of bone marrow aspirate specimens

Coagulation profile was done at baseline in all patients. Laboratory diagnosis of Disseminated Intravascular Coagulation (DIC) was based on changes in activated partial thromboplastin time, prothrombin time, fibrinogen degradation products (FDPs), and/or D-dimers.

Patients were classified according to the risk group as on the basis of WBC and platelet counts (PLT) at diagnosis-

- Low risk, WBC<10 × 10^9/L and PLT >40 × 10^9/L
- Intermediate risk, WBC<10 × 10^9/L and PLT < 40 × 10^9/L
- High risk, WBC>10 × 10^9/L

Treatment outcome:

Induction therapy, Induction therapy consist of ATRA 20 mg/m2/day, divided into two doses administrated every 12 hourlies, until CR (no longer than 90 days), along with As_2O_3 0.16 mg /kg /day for until hematologic CR or for a maximum of 60 days or Daunorubicin 60-90 mg/m2 (1-3 days). Anthracycline or Cytarabine (AraC) 100-200 mg/m2 (1-7 days) was added to the high-risk patient.

Consolidation therapy, In the low risk-group, 2-3 cycles of 15 days of ATRA 20mg/m2/day alone with As_2O_3 0.16 mg/kg/day for three cycles and high-risk group was also added IDA, HA for 3-4 cycles

Maintenance therapy:

In the low-risk patients, three months are one cycles and total of three cycles should be completed for nine months. PML-RARA should be checked after each cycle on three months. In the first months, ATRA given for two weeks and then two weeks rest. In the second months, ATO given for two weeks and then two weeks. In the third months, 6-MP is given and continued for whole months with no rest. In the high-risk patients, three months are one cycles and total of eight cycles should be completed for twenty-four months. PML-RARA should be checked after each cycle on three months. In the first month, ATRA given for two weeks and then two weeks rest. In the second month, ATO for two weeks and then two weeks rest. In the third month, ATO given for two weeks and then two weeks rest.

The patient was hospitalized for Induction therapy under closed supervisions and monitoring. Complete blood count (CBC) was done on every 3 days in Induction but if patients were symptoms present or high-risk group, then done every day. It is done weekly in Consolidation and at each subsequent visit in Maintenance and Follow-up.

Bone marrow analysis was done at the end of Induction when two sequential CBCs were consistent with Complete Remission (CR). If the bone marrow analysis showed evidence of persistent disease, then therapy was continued and the bone marrow analysis was repeated at weekly intervals until CR was achieved

or until the maximum duration of the induction period.

Coagulation parameters were monitored on the basis of FIB and related symptoms. If FIB was abnormal then done every day but if FIB was normal and no any related signs & symptoms then done every 3-4 days and also included a prothrombin time (PT), activated partial thromboplastin time (aPTT), and thrombin time (TT) performed by standard methods.

Fresh-frozen plasma (FFP) correction were given only when FIB <1.5g/l then given cryoprecipitate and if PT, aPTT are prolonged then transfused FFP + cryoprecipitate.

Liver function test, renal function test, and Electrolytes were done on the basis of patient's conditions, if patients was stable then weekly done and if the patient presents abnormal sign and symptoms then done every 3-4 days. Electrocardiogram (ECG) was done only if clinically indicated and also when given Arsenic Trioxide then weekly done. Patient with suspected ATRA syndrome, were treated with Dexamethasone 10 mg IV 12 hourly for at least 3 days and ATRA was discontinued.

CNS prophylaxis for given Lumbar puncture (LP), were given to each patient who achieved CR with combination of Cytarabine+ MTX+ Dexamethasone. Evaluation of response, Complete Remission was defined as normalization of peripheral blood counts (platelets >100 x 109/l, absolute neutrophil count >1 x 109/l) and a normocellular bone marrow with <5% blasts.

Failure was defined as an inability to achieve CR. Patients who died during or after induction chemotherapy who did not have a bone marrow examination were considered to be treatment failure. Remission duration was defined as the time from the attainment of CR to relapse, death during CR or to last follow up while in CR. Relapse was defined as the presence of >5% leukemic Promyelocytic or blast cell in the bone marrow, or appearance of leukemic cells in the peripheral blood or central nervous system. The toxicity profile was determined on the basis of physical examination, chest X-rays, electrocardiogram and determination of left ventricular ejection fraction by multi gated radionucleotide scan. A biochemical screening was performed before treatment and at least twice weekly during chemotherapy, toxicity was graded according to WHO criteria. ATRA syndrome was defined according to Frankel et al. [23]

Induction (N=38)	No. of patient (%)	CR (%)	Induction deaths (%)
ATRA+ATO	23 (61)	22 (96)	1 (4.3)
ATRA+D	12 (32)	10 (83.3)	2(16.6)
ATRA	3 (7.9)	3 (100)	0
Risk category			
Low	10	10 (100)	0
Intermediate	15	14 (93.3)	1(6.6)
High	13	11 (85)	2 (15.3)

Table 1: Treatment regimens and response

Definition of outcome:

Complete Remission (CR) was defined as normalization of leucocyte counts with normal differentiation, normal platelet counts, no organomegaly and normal marrow cellularity with <5% blasts plus Promyelocytic on bone marrow examination. OS was defined as the duration from the time of presentation to the time of death.

Statistical analysis:

Data was compiled and analyzed using the Statistical Package for the Social Sciences version 22.0 (SPSS Inc., Chicago, IL, USA). The analysis was done on the patients who were treated. The results were expressed as mean for quantitative variables and qualitative variables are presented as frequency & percentages. χ^2 (Pearson) test was used to compare differences between groups with respect to the number of the patients in each group, age, sex and response to therapy. The probability of survival was estimated with the use of the Kaplan and Meier method for overall survival, and disease-free survival and compared by the log-rank test among the three risk groups. All survival estimates are reported ± 1 SE. All *P* values were two-sided, with values of 0.05 or less indicating a statistical significance.

Smears of cases of APL:

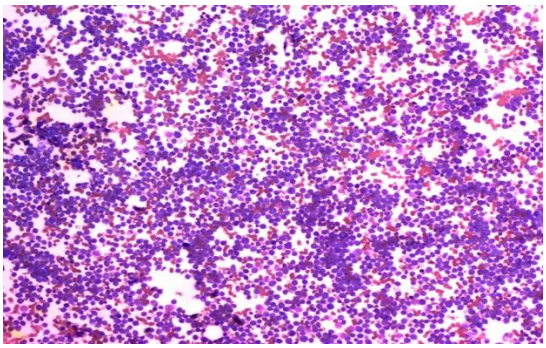

Figure 1: Bone Marrow Aspirate showing Hyper cellular.

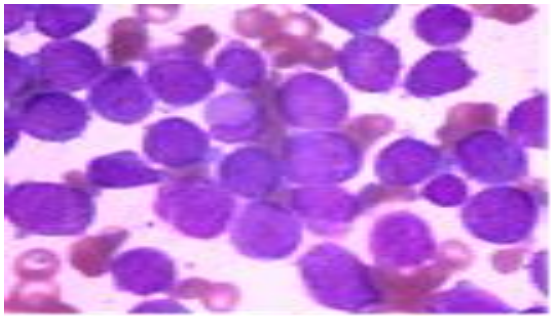

Figure 2: Bone Marrow Aspirate showing blast cells.

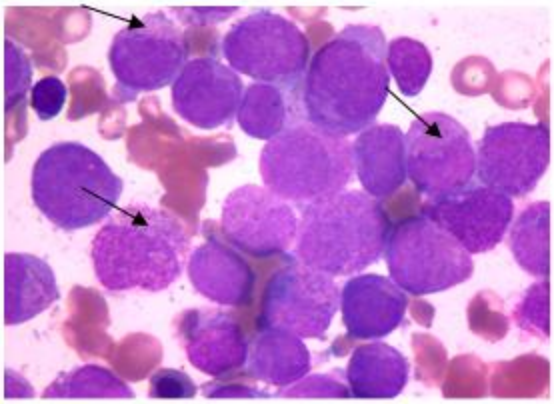

Figure 3: Bone Marrow Aspirate showing Auer rod (arrow).

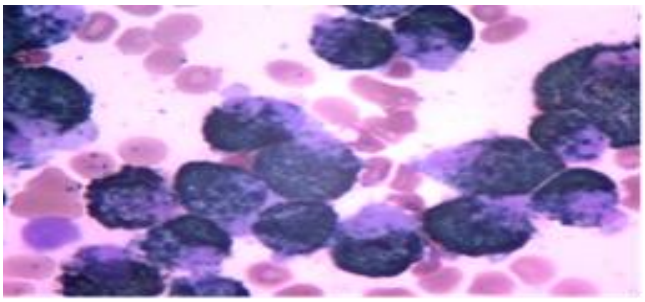

Figure 4: Bone Marrow Aspirate showing POX (Peroxidase) positive.

RESULTS

During the five years of study period at Dali University First Affiliated Hospital, Dali city, 38 patients were diagnosed with Acute Promyelocytic Leukemia. The patient characteristics are summarized in Table 2.

Out of 38 patients, 11 were Males (28.95%) and 27 were Females (71.05%) with a male to female ratio 1.9:1 (P value < 0.748). The mean age of patients was 38 years old with the median age of 39 years old (P value < 0.581). 37% of the diagnosed case was between ages below than 35 years old, 47% of the diagnosed case was between ages of 35 to 54 years old, 16% of a diagnosed case was between age above or equal to 54 years old. For ethnicity, 18 were Bai (48%), 13 were Han (34%), 3 were Lisu (8%), 2 were Yi (5%) and 2 were Tibetan (5%) peoples.

Occupation were Farmer in 24 (63.2%) patients, office workers in 5 (13%) patients, Student in 5 (13%) patients, Driver 1 (2.63%) patients, Civil servant in 1 (2.63%) patients, Teacher in 1 (2.63%) patients.

The major complaints were Fever in 23 (60.5%) patients, Cough in 13 (34%) patients, Epistaxis in 18 (47%) patients, Gingival bleeding in 21 (55%) patients, Petechiae in 27 (71%) patients, Ecchymosis in 24 (63%) patients, Fatigue in 25 (65.8%) patients, Joint pain in 14 (36.84%) patients, Dyspnea in 12 (31.6%) patients, Hepatomegaly in 13 (34%) patients and Lymphadenopathy in 7 (18%) patients.

The mean Hemoglobin was 9.5(range4.5-14.5) g/dl with a mean MCV of 89.26 fl. The total leukocyte count of 20.3297(range 4-10)/L; Absolute Neutrophilic count (ANC) of 37.26 and platelet count were

76.5(range100-300) /L.

Based on morphology, the diagnosis was established by detection of PML-RARA mutations by fusions proteins PML-RARA bcr1 in 15 (39.5%) patients, bcr2 in 12 (31.6%) patients, and bcr3 in 11 (28.5%) patients.

According to Gruppo Italiano Malattie Ematologiche dell'Adulto (GIMEMA) and PETHEMA risk stratification, 13 (34.12%) patients were in high-risk, 15 (39.47%) patients in intermediate risk, while 10 (26.32%)) patients in the low-risk group.

Thirty-eight patients received Induction therapy using either ATRA+ As_2O_3, n= 23 (61%) or ATRA + Daunorubicin, n= 12 (32%) and ATRA alone, n=3(7.9%). Following Inducting therapy, 35 patients achieved CR after first chemotherapy (92.1%) out of which 2(5.3%) patients died on after Achieved CR. Out of 3(8%) remaining patients, 1(3%) patients died within one week and 2(5.3%) patients died after two weeks of induction due to the complication of bleeding before receiving CR therapy as they delayed their scheduled follow up because of their own socio-economic problems. Thus, the CR rate for all 38 patients was 35/38= 92.1% (P value < 0.001).

All the 35 patients who achieved CR, Complication during Induction therapy with ATRA syndrome, n=2 (5.26%), Intracranial bleeding, n=4 (10.52%), DIC, n=5 (13.16). All patients were evaluated for toxicity. Majority of the patients had either grade I or II toxicity, mainly mucositis, vomiting, and diarrhea. Renal, Hepatic and Cardiac toxicity was seen in the occasional patient only.

ATRA Syndrome occurred in two patients (5.26%), the median day of onset of ATRA syndrome was day 8 of therapy (range 12-30 day). Most common features were dyspnea, pulmonary infiltrates and skin rash. Both patients responded to Intravenous Dexamethasone and discontinuation of ATRA.

Out of Thirty-eight patients, 25 patients developed febrile neutropenia, six patient developed chest infection, three patient developed oral cavity infection and eight patients developed skin and soft tissue infection.

Patients received Consolidation and Maintenance as per the protocol mentioned above. Out of 35 patients, one patients died during Maintenance therapy in other hospitals as per the request of the patient's relatives after CR in our hospitals. The remaining last patients died during Re-Induction (after relapse).

Patients who received CR to given consolidation chemotherapy using ATRA+ As_2O_3, 31(94%), As_2O_3, 2(6%), ATRA 3(10%), high dose ARAC 5(15.2%). Twenty-nine patients received maintenance chemotherapy; ATRA+ As_2O_3+6MP, 23 (70%), ATRA plus As_2O_3 6(18.1%).

The median duration of CR was 13 months (range 3-55 months); 19 patients are first CR, 6 patients second CR and 3 patients in third CR.

Summary of Admitted cases of APL:

Patient's characteristics	No of patient's (%)
Gender	
Male	11 (29%)
Female	27 (71%)
Ratio	1.9:1 F/M
Age group (Years)	
<35	14(37%)
Continued	
35-54	18(47.3%)
>54	6(16%)
Median age	39 years old
Race	
Bai	18(48%)
Han	13(34%)
Lisu	3(8%)
Yi	2(5%)
Tibetan	2(5%)
Occupation	
Farmer	24 (63.2%)
Office	5 (13%)
Student	5 (13%)
Driver	1 (2.63%)
Civil servant	1 (2.63%)
Teacher	1 (2.63%)
PML-RARA	
Bcr1	15 (39.5%)
Bcr2	12 (31.6%)
Bcr3	11 (28.5%)
Risk category	
Low	10(26.32%)
Intermediate	15(39.47%)
High	13(34.21%)
Clinical features	

Fever	23(60.5)
Continued	
Cough	13(34
Epistaxis	18(47)
Epistaxis	18(47)
Gingival bleeding	21(55)
Petechiae	27(71)
Ecchymosis	24(63)
Fatigue	25(65.8)
Joint pain	14(36.84)
Dyspnea	12(31.6)
Hepatomegaly	13(34)
Lymphadenopathy	7(18)
Lab parameters	
DIC positive	5(13.15)
Abnormal renal functions	4(10.53)
Abnormal liver functions	3(7.9)
Abnormal chest X-ray	14(36.8
****CBC**	**Mean**
Hemoglobin (range) gm/dl	95.5 (110-150)
WBC (range) per L	20.3297($4x10^9$/L)
Platelets (range) per L	76.5000(100-300 $x10^9$)

Table 2: Patient's characteristics (N=38)

- Cases of APL were further divided on the basis of Gender which is listed below on the (Table 3) and (figure 5)

Gender	Cases of APL
Male	11
Female	2

Table 3: Division of APL in the basis of Gender

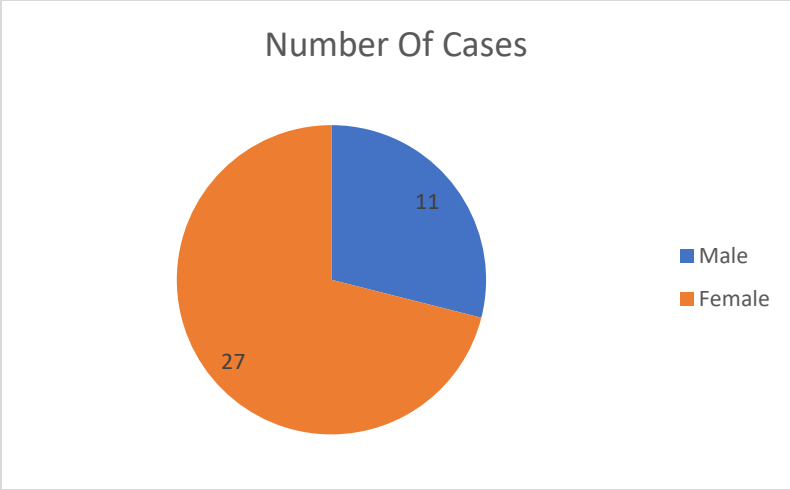

Figure 5: Division of APL on the basis of Age Group

- Cases of APL was divided into according to the Age Group into three groups which are listed below on (Table4) and (figure 6)

Age Group (in years)	Cases of APL
<35	14
35-54	18
> 54	6

Table 4: Division of APL on the basis of age group

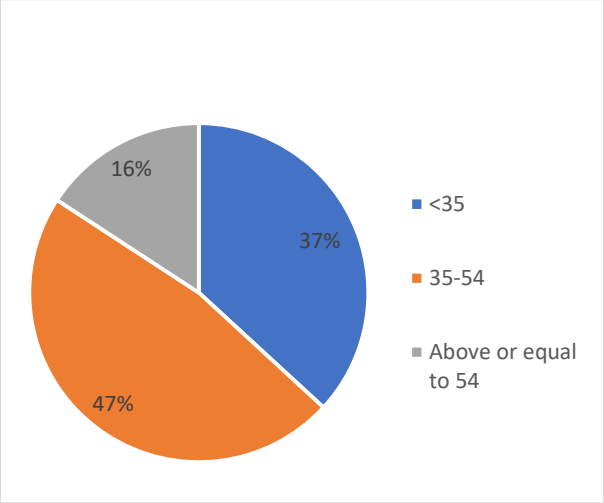

Figure 6: Division of APL on the basis of Age Group

- Comparisons between different Ethnic groups for APL patients which are listed below on the (Table 5) and (figure 7)

ETHNICITY	Cases of APL
Bai	18
Han	13
Lisu	3
Yi	2
Tibetan	2

Table 5: Division of APL on the basis of Ethnicity Group

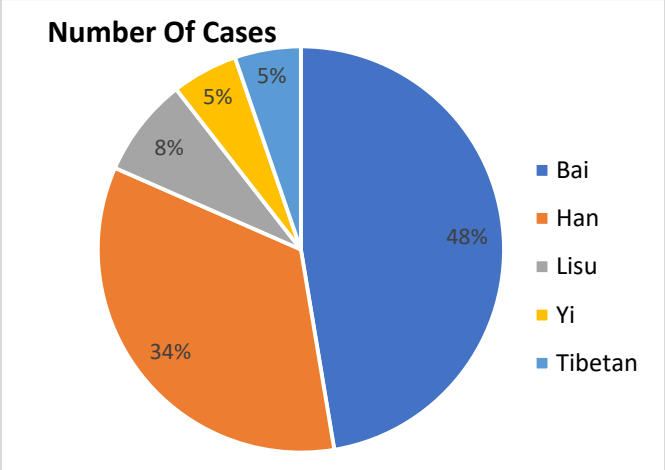

Figure 7: Division of APL on the basis of Ethnicity Group

- Clinical features associated with cases of APL are due to Anemia, Thrombocytopenia, and Leukopenia which can be listed below on (Table 6) and (figure 8)

Clinical Features	Present in Cases of APL
Fever	23
Cough	13
Dyspnea	12
Epistasis	18
Gingival Bleeding	21
Petechiae	27
Ecchymosis	24
Fatigue	25
Joint pain	14
Lymphadenopathy	13
Hepatomegaly	7

Table 6: Division of cases in the basis of clinical features

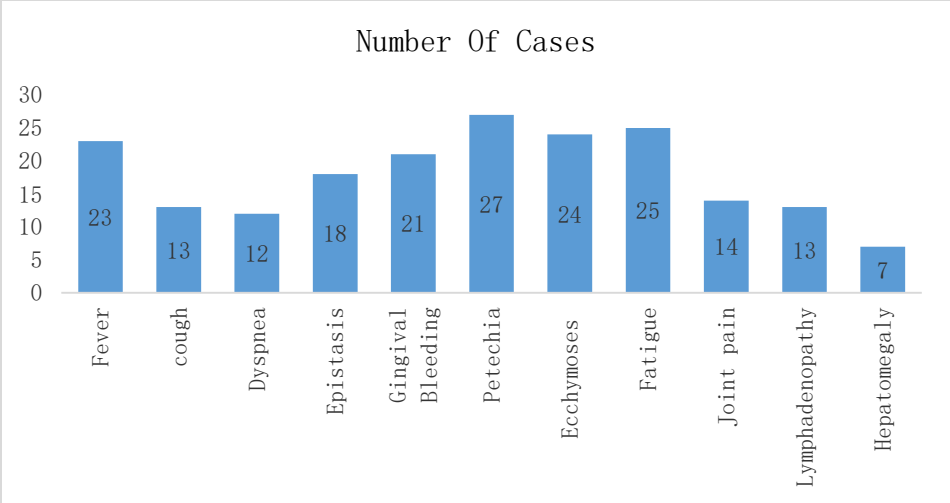

Figure 8: Division of cases in the basis of Clinical features

- Patients were classified according to the Risk Category on the basis of WBC and Platelet counts (PLT) at diagnosis (Table7) and (figure 9)

Risk category	Number of patients
Low risk, WBC<10 × 10^9/L and PLT >40 × 10^9/L	13
Intermediate risk, WBC<10 × 10^9/L and PLT < 40 × 10^9/L	15
High risk, WBC>10 × 10^9/L	10

Table 7: Division of cases in the basis of risk category

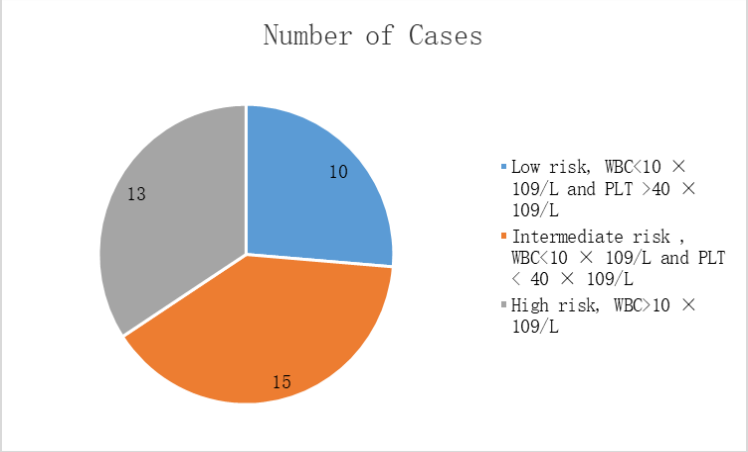

Figure 9: Patients were classified according to the Risk Category

- Patients were classified according to the complication table 7 and figure 10.

Complication	Number of patients
Intracranial hemorrhage	4
DIC	5
Retinoic Acid Syndrome	2

Table 8: Divisions of cases in the basis of complication

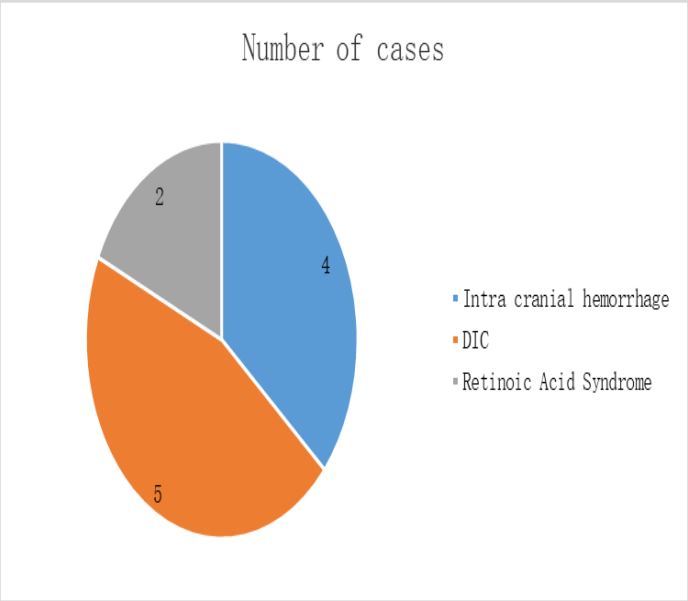

Figure 10: Patients were classified according to the Complication

Comparison of our data with data of others published an article about APL

Author	Year	Country	No. of patients	CR%	OS%
Present study	2018	China	38	92	87 (5 years)
Karthik Udupa et al [22].	2017	India	12	80	
Ya fang Ma et al [23].	2016	China	585	95	95
Dayama A et al [24].	2015	India	34	88.23	75.45±7.6 (4 years)
Fang Xu et al [25].	2014	China	72	91.1	
F. Lo-Coco et al [26].	2013	Italy	231	ATRA+AS2O3 = 100	
Bajpai, et al [2].	2011	India	43 (33treated)	81.81	75.13 ± 8.51
Mathews et al [27].	2010	India	72	86	74.2% ± 5.2(5 y)
Rafael et al [28].	2007	Brazil	157	72.85	23.5 months
Asou et al [29].	2007	Japan	283	94	83.9 (6 y)
Mathews et al [30].	2006	India	72	86.1	86.11± 4.08 (3 y)
Sanz et al [31].	2004	Spain	426(79) *	90	
Iland et al [32].	2003	Australia	101	90	88 (5.7 y)

Bourgeois et al [33].	2003	France	576	2.5	77-84 (5 y)
Tallman et al [34].	2002	USA	350	ATRA70; DA73	69 (5 y), 45 (5 y)

OS= Overall survival, *Low risk (WBC count <10 × 109/L; platelet count <40 × 109/L). LPA96, CT in consolidation therapy. LPA99, CT+ATRA in consolidation therapy.

DISCUSSION

In this study, we retrospectively reviewed a series of 38 APL cases followed at our Institution including their age, gender, ethnicity, clinical features, hematological complications, BM morphological and risk stratification profiles. Baseline characteristics of these patients are similar to early report.

APL is most commonly found in the Age group between 30-40 years old in our studies. The median of Age group is found to be 39 years old. Previously, reported by other data form Pakistan, has reported a median age of 41 years old, which is a little bit high as compared with our findings. This difference might be the reflection of the fact that past study was conducted exclusively on adult's patients [7]. However, large regional studies reported from China has shown the median age of 33 and 40 years respectively [11, 12, 13].

The APL epidemiological features have described, no gender predilection [7]. However, we determined the female gender dominance F/M 1.9:1, which was also seen in Malaysian APL patients [14]. Similar findings were among the female gender in one large cohort of 1400 patients from USA [15].

The Clinical manifestations of APL are heterogeneous, patients are usually symptomatic. Patients often had hemorrhagic diathesis, fever, general malaise or thrombotic. Most of our patients had active bleeding as a predominant symptom (69%). This is more or less similar to studies reported from India (70%); Egypt (79%) and Italy (90%) [2, 16, 17].

ATRA and combination of ATO chemotherapy were used for remission induction in APL patients and 96% achieved CR but for overall combination of induction chemotherapy 92.1% (P value < 0.001) . This is the similar study in multicenter trials, 91% in APL 91, 92% in APL 93, 95% in the Italian and 89% in the Japanese trials [18, 19, 20, 21]. These CR rates were superior to 69% - 81% CR obtained with chemo therapy (CT) alone, in our patients ATRA alone CR rates is 100%.

Comparisons of CR and OS between the present study and the prior reported in different literature is provided in Table 9. Table shows that the CR rate and the OS achieved were similar to other literatures.

In consolidation therapy, low risk patients we have used ATRA for two weeks with a total of one course plus As_2O_3 for three cycles and High-risk group was given IDA, HA for 3-4 cycles, may be associated with less morbidity. Use of intermittent ATRA, ATO and 6-Mercaptopurine maintenance therapy has shown to reduce the risk of relapse [35-37, 27].

In recent study it was found that, Combination of ATRA and ATO were given for induction and consolidation therapy is possibly superior. Comparing ATRA and ATO with ATRA and CT(chemotherapy), Lo-Coco et al have reported 100% CR with two years EFS of 97%. This was better than the ATRA and CT [26].

Total mortality was 13.2 % due to bleeding and sepsis, 8% during induction therapy and 5.3% due to after

achieved CR of our patients. The early death rate with APL reported in the literature vary widely, like 40% [38], 32% [39], 15% [40] and 10.1 % respectively [31]. In our study, the most common type complication was DIC, which was observed in 5(13%) patients and conformed by laboratory test. De le serna et al reported that the most common cause of early induction death was intracranial hemorrhage [41]. All our patients with hemorrhage had low platelet counts, with a mean platelet count of 15 × 109/L and a mean fibrinogen level of 198 mg/dl. Our findings suggest that due to the high risk of bleeding diathesis in patients with APL, our aim for higher platelet count of around 50 × 10^9/L during induction therapy, which may help to prevent death from hemorrhage.

The incidence of ATRA syndrome has varied from 6 to 27% in various studies. In our study ATRA syndrome occurred in 5.3% of patients. The patients responded to dexamethasone and discontinuation of ATRA and no mortality was encountered. Which was similar study to Bajpai et al [2] and sanz et al [24]. Over representation of high risk patients & a lower threshold for diagnosis may be responsible for the high incidence of suspected ATRA syndrome observed in our study.

The majority 39.5% of patients with APL in our study belonged to the intermediate-risk category, with WBC<10 × 10^9/L and PLT < 40 × 10^9/L at the time of diagnosis. While only 26.32% were in the high-risk group, with WBC<10x10^9/L. High risk patients were compared with Bajpai et al. 23% [2], 53% and 23% GIMEMA and PETHEMA groups [8]. This is little difference between our study and the western studies.

During our study conducted over 38 Chinese patients, according to ethnicity, APL was found mostly in the people from Bai group (48%) followed by Han Group (34%). Least group affected from APL were Lisu, Yi and Tibetan which was 8%, 5% and 5% respectively. However no studies have been conducted over Ethnic variation and APL.

This disease is considered to be mostly associated with low socio-economic status. In our study conducted over 38 Chinese patients, the disease APL was found to be most in 24 patients (63.2%) and least in civil servants and teachers around 2.63% of patients. Similarly no studies and research have been done which shows relation over occupation and APL.

In our study conducted, overall survival rate for APL patients is found to be 87% (P value < 0.22) and DFS is 90% (P value =1).

Our study had its share of limitations, the late presentation was a problem encountered in our center. In developing countries such as ours, patients tend to first be treated by local physicians and are usually referred quite late to tertiary-care centers due to patient's inadequate awareness of the seriousness of the disease and socio-economic conditions, which results in delayed diagnosis and initiation of therapy. Furthermore, many of our patients only presented to our center after being treated at the primary care center.

We recognize the limitations of our results since this is a retrospective report of a relatively small series of patients observed and treated in a single centre. Therefore, these results need to be confirmed prospectively in a larger series. However, the CR rate and OS are encouraging and suggest that despite the

limited resources available in developing countries APL patients can still achieve outcomes comparable to international standards.

CONCLUSION

- ATRA+ATO is the best treatment for APL. In our study 38 patients received Induction therapy, In 23 patients we used ATRA+ATO and the CR was 96%, in 12 patients ATRA+ Daunorubicin was used and CR was 83.3% and in 3 patients ATRA alone was used and the CR was 100%.
- The incidence of APL is slightly higher in female populations in our study.
- APL is most commonly found in the age group between 30-40 years in our study. The median age group is found to be 39 years.
- Fever, cough, epistaxis, gingival bleeding, petechiae, ecchymosis, fatigue, joint pain, dyspnea, hepatomegaly, lymphadenopathy are the predominant clinical features at the time of detection of APL.

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