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612.ACUTE LYMPHOBLASTIC LEUKEMIAS: CLINICAL AND EPIDEMIOLOGICAL

Acute Lymphocytic Leukemia (ALL) in Pregnancy, Case Report and Literature Review

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Introduction: Leukemia is rare in pregnancy, occurring in up to 1 in 100,000 pregnancies. A 28F G2P1 was diagnosed at our institution with Philadelphia (Ph) negative B-ALL at 24 weeks' gestation. She was induced with UKALL14 and achieved a flow negative complete remission post-induction. During induction chemotherapy, regular ultrasound scans showed that the fetus was growing normally for gestational age. The patient was kept on weekly vincristine and prednisone and had an elective c-section at 31+3 weeks, in light of her previous caesarean section, poor bishop score, and in order for her to safely resume chemotherapy. Baby girl had an uneventful hospital course and was discharged after 29 days. Given the sparse data on this challenging topic, we decided to review the literature for all reported cases of ALL in pregnancy.

Methods : We reviewed the literature for all reported cases of ALL from 2000 to 2023. We collected available data on the patient, pregnancy, and fetal outcome as well as leukemia characteristics and chemotherapy received.

Results: We found 57 patients across 20 studies. The median age at diagnosis was 26 years (range 16-41 years). Most affected pregnancies were during the second trimester (T2) (n 23/57) and third trimester (T3) (n 20/57). The subtype of ALL was reported in 49 patients; of those, B ALL was the most common (n 35/49). Ph was reported positive in eight patients. A total of 53 patients received chemotherapy, of those 33 patients were received during pregnancy, while 13 were after pregnancy, and the remaining 7 had unclear timing. Patients received different combinations of standard ALL chemotherapy agents including vincristine (n 49/53), cyclophosphamide (n 25/53), prednisone (n 42/53), dexamethasone (n 23/53), L-asparaginase (n 20/53), pegaspargase (n 1/53), daunorubicin (n 36/53), doxorubicin (n 7/53), idarubicin (n 4/53), cytarabine (n 11/53), 6-mercaptopurine (n 8/53), cytosine arabinoside (n 1/53), and methotrexate was given to 8 patients intrathecally during pregnancy; 6 during T2 and 2 during the first trimester (T1). Dasatinib and imatinib were given to two patients at 33 and 24 weeks respectively. There were no reports of patients who were treated with immune therapy while pregnant.

All four patients who did not receive any treatment died from progressive disease. Complete remission (CR) was reported in 45 patients. One patient died during induction from septicemia, five were refractory to induction chemotherapy and 2 did not have induction outcome reported. Of those who achieved a CR, 21 were reported alive and 16 reported dead at last follow up. Among those mortalities, 8 were due to relapsed leukemia, 3 due to infectious causes, 2 due to respiratory failure and 2 from unspecified causes. Five patients were reported to have persistent or refractory leukemia, 4 of whom died.

Among the 14 T1 pregnancies, 10 were terminated electively, 3 spontaneously, and there was one maternal death due to declining treatment. Three patients received chemotherapy during T1, two suffered a spontaneous abortion and one had a missed miscarriage. Among the 23 T2 pregnancies, 17 resulted in live deliveries, one stillbirth during chemotherapy, one maternal death and 4 spontaneous abortions; 2 of which received chemotherapy during pregnancy, one did not receive treatment and one abortion with unclear timing of chemotherapy initiation. Among the 20 T3 pregnancies, 19 had successful deliveries and one stillbirth at an unindicated gestational age after receiving chemotherapy. Five babies were reported to have low birth weight, four had neonatal cerebral ischemia, one had intraventricular hemorrhage and one suffered from intestinal

obstruction 2 weeks after delivery. All babies were discharged from hospital with no adverse congenital or developmental complications.

Conclusion : Treatment of women presenting with ALL at or beyond T2 is possible with high early remission rates for the mothers and delivery of healthy babies. The outcome is highly dependent on the gestational age. It is important that more cases are reported on this topic due to its challenging and multidisciplinary nature especially given the sparse data available and potential for reporting bias.

Disclosures No relevant conflicts of interest to declare.

PI #	Short Reference	Year	Maternal Age (years)	R: T cell	FR: tv/r	Molecular	GA at Dx (weeks)	Course of pregnancy	Pregnancy outcome	GA at delivery	Fetal outcome	Chemotherapy	Induction (chemotherapy) during pregnancy or after delivery	Response to induction therapy	Fetal outcome	Survival after diagnosis
1	Kobayashi, Shoji et al.	2023	33	ab-r	ab-r		33		Delivery - CS	34-1	live birth	Daunorubicin + etoposide	during	CR	Alive (Auto-SCT)	24 months
2	Kobayashi, Shoji et al.	2023	36	ab-r	ab-r		35 (relapse)	PTSDM	Delivery - VSD	34-4	live birth	Allogeneic (CPM, VCR, ADX, DEXA)	during	CR	Dead	32 months
3	Zhu D et al.	2022	33	B ALL	ab-r		34		Delivery - CS	term	live birth	DNR + VCR + CPM + PRED	during	CR	Dead from Pulmonary infection	8 months
4	Zhu D et al.	2022	41	B ALL	ab-r		27		Delivery - VSD	preterm	live birth	DNR + VCR + CPM + PRED	during	CR	Dead from refractory leukemia	16 months
5	Zhu D et al.	2021	39	B ALL	ab-r		34									
6	Vijay-Kumar A, Jena MC, Moh E, et al.	2018	37	T ALL		T(12;21)(p13;q14) TELX1 translocation with a complex karyotype	36		Delivery - VSD	37-2	live birth	PRED prophylaxis	during	CR after remission induction chemotherapy	Alive	-
7	Parham N, et al.	2017	26	B ALL		T(12;21)(p13;q14) + t(1;19)(q23;p11)	32		Active termination	34 wk	miscarriage	CT1001 young adult protocol of VCR, ADX, PRED, CPM, L-ASP	after	Partial	Alive	-
8			23	B ALL			6		Spontaneous abortion	7 wk	miscarriage	VCR, ADX, PRED, CPM, L-ASP	after	CR	Alive	-
9			34	Ph B ALL	Ph-r		33		Spontaneous abortion	18 wk	miscarriage	CPM, L-ASP, DNR, PRED	during	CR	Dead from septic shock + resp failure (post Auto-SCT)	4 months
10			19	ALL t(1;19)		NDKX + X, X, +4, +19, +14, +17, -18, -21, -21	30	Stillborn	stillborn	22 wk	Dead	DNR + PRED + VCR	during	CR	Dead from sepsis failure	11 months
11			28	B ALL		unknown	35		Delivery - VSD	38 wk	live birth	DNR + PRED + VCR	after	CR	Dead - refractory ALL	11 months
12	Mahor C, et al.	2016	38	B ALL	Ph-r		24	Maternal lymphomatous profile	Delivery - CS	36	live birth, low birth weight	Allogeneic (CPM, DEXA, VCR, VCR, CTR, etoposide)	during	Not reported	Dead from sepsis and renal failure	-
13	Sekih A, et al.	2014	33	Ph B ALL			30		Delivery -	38 WK	live birth	None			Dead from progressive disease	-
14			22	Ph B ALL		CPX, X, X(17;22)(q21)	32		Spontaneous abortion	17 wk	miscarriage	None			Dead from progressive disease	-
15			26	Ph B ALL			28		Spontaneous abortion	14 wk	miscarriage	VCR, ADX, PRED, CPM, L-ASP	during	CR	Alive (SCT)	-
16			23	Ph B ALL			33		Spontaneous abortion	14 wk	miscarriage	None			Dead from progressive disease (post SCT)	-
17			17	Ph B ALL		inv(16)(p11q23)	29		Delivery -	38	live birth	VCR, ADX, PRED, CPM, L-ASP	during	CR	Alive	-
18			20	T ALL		inv(16)(p11q23)	31		Delivery -	33	live birth	VCR, PRED	during	CR	Dead from progressive disease (post SCT)	-
19	Khandaker S, Moshir S	2014	25				26	paternal neoplasia genes (Vaccinator + MTX + mesoparasit)	Delivery - CS	34 wk	live birth	DEXA, PRED, MTX (IT), VCR, L-ASP	during	CR	Alive	-
20	Zaid, A et al.	2014	34	B ALL			9		Spontaneous abortion	16 wk	miscarriage	DNR, VCR, ASP, PRED, MTX (IT)	during	morphologic remission	Dead from pulmonary hemorrhage	27
21	Ticks, F et al.	2013	32	B ALL	ab-r	NDKX, X(22)(p14q12)	26		Delivery - CS	38 wk	live birth	Allogeneic (CPM, VCR, ADX, DEXA)	during	morphologic remission	Alive	-
22						NDKX, X(22)(p14q12), X(1;22)(p11q23), X(1;19)(q23;p11), X(9;22)(q34;q13), X(1;21)(q21;q21), X(11;22)(p15;q14), X(11;22)(q24;q24), X(11;22)(q24;q24)	27		Delivery - CS		live birth					
23	Nakajima Y, et al.	2013	36		Ph-r		27		Delivery - CS	32-1	live birth	DNR, VCR, CPM, PRED	during	CR	Alive	730 days
24	Reinhold Miller J, et al.	2011	27	Ph B ALL	ab-r		28		Delivery - CS	38	live birth	VCR, DNR, mesoparasit, PRED, CTR (IT), MTX (IT)	during	CR	Alive	-
25	Aghaj, M et al.	2009	37	Ph B ALL		X(11;22)(q23;q24)	29		Delivery - VSD		live birth, anemia	VCR, DEXA, DNR, ASP	during	CR	Dead after relapse (refractory), relapsed SCT	-
26	Aghaj, M et al.	2009	35	Ph B ALL		X(11;22)(q23;q24)	34		Spontaneous abortion		miscarriage	VCR, DEXA, DNR, ASP	after	CR	Dead - Primary refractory	-
27	Aghaj, M et al.	2009	21	Ph T ALL		Normal karyotype	30		Delivery -		live birth, anemia	VCR, DEXA, DNR, ASP	after	CR	Dead - relapse 4 months after CR and 10 months post Auto-SCT	-
28	Aghaj, M et al.	2009	27	Ph B ALL		X(11;22)(q23;q24)	31		Active termination	33	miscarriage	CPM, VCR, DEXA, DNR, ASP	after	CR	Dead - relapse 3 years post Auto-SCT	-
29	Aghaj, M et al.	2009	27	Ph B ALL		Non informative	33		Spontaneous abortion	34	miscarriage	Not indicated	during	CR	Alive (Auto-SCT)	4 years
30	Perenchikovs DN, et al.	2009	30	B ALL	Ph-r		30		Active termination	38 wk	miscarriage	PRED, DEXA, DNR, VCR	after	CR after 1st induction	Dead due to refractory relapse	-
31	Perenchikovs DN, et al.	2009	22	T ALL	Ph-r	MEL-r	39		Active termination	33 wk	miscarriage	PRED, DEXA, DNR, VCR, CPM, CTR, DDP	after	CR after 2nd induction	Alive (Auto-SCT)	-
32	Perenchikovs DN, et al.	2009	28	T ALL	Ph-r	NDKX, MEL-r	39		Active termination	38 wk	miscarriage	PRED, DEXA, DNR, VCR, CPM, CTR, DDP	after	CR after 2nd induction	Alive (Auto-SCT)	-
33	Perenchikovs DN, et al.	2009	23	T ALL	Ph-r	NDKX, del(11)(q23)	35		Delivery - CS	35 wk	live birth, IVL, NCI	PRED, DEXA, DNR, VCR	after	CR after 1st induction	Dead due to refractory relapse	-
34	Perenchikovs DN, et al.	2009	18	B ALL	Ph-r	NDKX, MEL-r	36		Delivery - CS	38 wk	live birth	PRED, DEXA, DNR, VCR	after	refractory	Dead due to refractory ALL	-
35	Perenchikovs DN, et al.	2009	24	B ALL	Ph-r	del(11)(q23)	40		Delivery - VSD	40 wk	live birth	PRED, DEXA, DNR, VCR	after	CR after 1st induction	Alive (Auto-SCT)	-
36	Perenchikovs DN, et al.	2009	25	T ALL	Ph-r	MEL-r	33		Delivery - CS	33 wk	live birth, intrauterine abortion at +1	PRED, DEXA, DNR, VCR, CPM, CTR, DDP	during	CR after 2nd induction	Alive (Auto-SCT)	-
37	Perenchikovs DN, et al.	2009	29	T ALL	Ph-r	del(11)(q23)	39		Delivery - CS	39 wk	live birth, SGA	PRED, DEXA, DNR, VCR, CPM, CTR, DDP	during	refractory	Dead due to refractory ALL	-
38	Perenchikovs DN, et al.	2009	35	B ALL	Ph-r	NDKX, MEL-r	39		Delivery - CS	39 wk	live birth	PRED, DEXA, DNR, VCR, CPM, CTR, DDP	during	CR after prod phase	Alive	-
39	Perenchikovs DN, et al.	2009	32	T ALL	Ph-r	NDKX, MEL-r	25		Delivery - CS	34 wk	live birth, NCI	PRED, DEXA, DNR, VCR, CPM, CTR, DDP	during	CR after extended 2nd induction	Alive (Auto-SCT + Auto-SCT)	-
40	Perenchikovs DN, et al.	2009	21	B ALL	Ph-r	del(11)(q23)	26		Delivery - VSD	36 wk	live birth	PRED, DEXA, DNR, VCR	after	CR after 1st induction	Alive	-
41	Perenchikovs DN, et al.	2009	26	B ALL	Ph-r	NDKX, del(11)(q23)	28		Delivery - CS	34 wk	live birth	PRED, DEXA, DNR, VCR, CPM, CTR, DDP	after	CR after 1st induction	Dead in CR due to septic shock	-
42	Perenchikovs DN, et al.	2009	29	B ALL	Ph-r	del(11)(q23)	30		Delivery - CS	36 wk	live birth, SGA, NCI	PRED, DEXA, DNR, VCR, CPM, CTR, DDP	after	CR after 1st induction	Alive (Auto-SCT)	-
43	Perenchikovs DN, et al.	2009	29	T ALL	Ph-r	MEL-r	31		Delivery - VSD	36 wk	live birth	PRED, DEXA, DNR, VCR	after	CR after 1st induction	Alive	-
44	Perenchikovs DN, et al.	2009	41	T ALL	Ph-r		31		Delivery - CS	38 wk	live birth, NCI	PRED, DEXA, DNR, VCR	after	CR after 1st induction	Alive	-
45	Pyppantina N, et al.	2008	36	B ALL		presence of nucleosome Nq9/9(4) and the deletion of the short arm of chromosome 9, region 9p21	26		Delivery - CS	32-4 wk	live birth, SGA	Concomitant ALL with presence of M (PRED, VCR, DNR, ASP, MTX (IT))	during	CR after phase 2	Alive	18 months
46	Mamuda, C et al.	2007	36	B ALL			26		Delivery - CS	32	live birth, SGA	DNR, VCR, ASP, PRED, MTX (IT)	during	CR	Alive	29 months
47	Middendorp, J P M et al.	2005	30	ab-r	ab-r		4	Maternal miscarriage	Active termination	11	miscarriage	PRED, VCR, ASP, DNR, MTX (IT)	during	remission leukemia	Dead after stem cell transplant secondary to sepsis + ARDS	-
48	Middendorp, J P M et al.	2005	37	ab-r	ab-r		15		Spontaneous abortion	22 wk	miscarriage	PRED, VCR, ASP, DNR, MTX, After 3 wks CTR	during	remission leukemia	Dead	-
49	Chelphom V, et al.	2005	16	T ALL			17		Delivery - VSD		miscarriage	DNR, VCR, CPM, PRED	after	CR	refractory	-
50			14	Ph B ALL			6		Active termination		miscarriage	DNR, VCR, CPM, PRED	after	CR	Not clear	-
51			13	Ph B ALL			26		Delivery - CS		miscarriage	DNR, VCR, ASP, PRED	after	CR	Not clear	-
52			30	B ALL	Ph-r		18		Active termination		miscarriage	DNR, VCR, CPM, PRED	after	CR	Not clear	-
53			21	Ph B ALL			28		Delivery - CS		miscarriage	DNR, VCR, CPM, L-ASP, PRED	after	CR	Not clear	-
54			25	T ALL			9		Active termination		miscarriage	DNR, VCR, CPM, PRED	after	CR	Not clear	-
55			31	B ALL			18-31		Delivery - CS	38-31	live birth	VCR, DNR, PRED, L-ASP	after	CR	Dead from sepsis	18 days
56	Trenk MC, et al.	2001	39				18	mother died in CR during pregnancy	miscarriage						Dead from ARDS in CR	1.4 months
57	Hansen WT, et al.	2001	24	B ALL			24		Delivery - VSD	38 wk	live birth	unspecified	after	CR	Dead	16 months
58									Delivery - VSD		live birth	Concomitant leukemia Group B study 993 PRODUCTION CPM, VCR, PRED, DNR, L-ASP followed by 2 cycles of MTX (IT), CPM, DDP, CTR, VCR, L-ASP	during	CR after induction	Alive	-

Figure 1

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