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Original Research Article

Donor with Cen B Motifs and High KIR B Gene Motifs Contents has a Better HSCT Outcome in Pediatric Patients

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Abstract: Background: The aim of the study was to see the influence on the outcome of Hematopoietic Stem Cell Transplantation (HSCT) with Killer Cell Immunoglobulin like Receptor (KIR) mismatching. HSCT is the main mode of treatment for different Hematological Malignancies, Solid Tumors and Autoimmune Diseases. **Procedure:** Around 65 patients with different Hematological Malignancies were taken from Hospital Databases who underwent Allogenic HSCT from 2012 to 2018 with median age 8yrs(1yr-15yrs). Centromeric B (Cen B) motifs donor and Non Cen B motifs (Centromeric A/A) donor were evaluated and their outcome in HSCT was considered. As for the KIR B Motifs contents, they were evaluated on the basis of greater than 2 or less than 2 and their outcome on HSCT was considered. **Results:** In this study we found that Cen B motifs donor had the higher survival and relapse protection for pediatric hematological malignancies (DFS 56.482, 95% confidence interval 51.763-61.201, p=0.034) (RR 0.242, 95% confidence interval 0.056-1.056, p=0.044) compared to Non Cen B motifs donor. Donor with greater than two KIR B gene motifs contents had a better survival outcome and less relapse (DFS p=0.027) (RR 0.778, 95% confidence interval 0.665-0.909, p=0.025) compared to KIR B gene motifs contents less than two. **Conclusion:** KIR genotyping of several best HLA-matched potentials related and unrelated donors should substantially increase the frequency of better outcome in transplants by using grafts with favorable KIR gene content, KIR mismatching between donor and recipient, selecting donor with Cen B motifs and KIR B gene motifs greater than two.

Keywords: Centromeric B motifs, DFS, HSCT, KIR B gene motifs, KIR mismatching.

Abbreviation:
DFS: Disease free Survival; OS: Overall Survival; Cen B motifs: Centromeric B motifs; Tel B motifs: Telomeric B motifs; KIR: Killer cell immunoglobulin like receptor; HSCT: Hematopoietic stem cell Transplantation; PB: Peripheral Blood; CB: Cord Blood; CR: Complete Remission; GvHD: Graft versus Host Disease.

INTRODUCTION

Hematological disorders are common problems in pediatric group of population. Due to the growth and development in the modern technology most of the diseases that were thought to be incurable are now cured. Hematopoietic Stem Cell Transplantation (HSCT) has become the major backbone in the treatment of the most common and rare hematological and immunological diseases from hematological diseases, solid tumors to many immunological diseases [1]. Once thought to be the form of rescue therapy to support high-dose radiation and chemotherapy in the treatment of leukemia, now has become the major backbone of treatment for many diseases. More the patients are in need for HSCT, more new techniques are required to make it safer and more efficient. Most researches are dedicated towards its pre-transplantation assessments for getting best outcome like Overall survival (OS), Disease free survival (DFS) and reducing post-transplantation complications like Transplant related mortality (TRM), Relapse, Graft rejection, Acute

Graft versus Host Diseases (aGvHD) and Chronic Graft versus Host Diseases (cGvHD). Selection of the Donor on the basis of Human Leukocyte Antigen(HLA) compatibility is the most important but Age, Sex, parity,

Cytomegalovirus Serostatus, ABO blood type and Cell dose also plays an important role in HSCT outcome [2].Donor selection on the basis of these criteria has long being in practiced and many institutions have adapted to Killer cell immunoglobulin like receptor(KIR) genotyping and KIR ligand status for finding the donor on the basis of KIR mismatching. As the number of patients increases for receiving a transplant, there is a possibility that there are less chances of finding Donor with perfect HLA match. So this led to the evolvement of new methods, that led to the possibility of allogenic HSCT from HLA mismatched Donor. HLA mismatching led to high chances of Graft versus Host Disease (GvHD), so to overcome this problem Myeloablative HSCT became the mode of transplant, but myeloablative regimen increases toxicity and were not suitable for old morbid patients, so non-myeloablative or reduced intensity regimen were used, but that led to increase in relapse of the diseases. So, research went towards finding the method to overcome these problems, so alloreactivity of Natural Killer cells (NK cells) was thought to be the possibility for solving these problems. After Myeloablative HSCT, GvHD was controlled and NK cell alloreactivity led to the Graft versus Leukemia (GvL) effect towards Graft versus Host(GvH) direction. Many studies have shown the better HSCT outcome while some studies have shown the worse HSCT outcome by KIR mismatching [3]. KIR mismatching as the term implies is the method in which mismatching in the KIR between the patients and donor on the basis of Perugia KIR ligand model(Ligand-ligand mismatch: ligand present in donor that the recipient lack) [4], the Memphis receptor-ligand model (Receptor-ligand mismatch: receptor of the ligand present in donor that the recipient lack) [5] and Nantes model Receptor-receptor mismatch(receptor present in donor that the recipient lack) [6]. Stanford KIR haplotype model [7] is also consider as Receptor-receptor mismatch model as Nantes model is considered as the prototype of the Stanford KIR Haplotype Model [3]. Cen B and KIR B motifs contents are also related to Haplotype model as each Haplotype contains Centromeric and Telomeric part and they are further divided into Centromeric A(Cen A) i.e. Centromeric A1, Cen B i.e. Cen B1 and Cen B2 , Telomeric A(Tel A) i.e. Telomeric A1 and Telomeric B i.e. Telomeric B1[7-10]. Aim of this study was to see KIR mismatching in HSCT outcome in Pediatric Group of Patients.

Some of the researches have shown promising results with KIR mismatching and HSCT outcome. Compared with A Haplotype motif, Centromeric B (Cen B) and Telomeric B (Tel B) motifs both contributed to relapse protection and improved survival, but Cen-B homozygosity had the strongest independent effect and reduced relapse was achieved with donors having 2 or more B gene-content motif in Acute Myeloid Leukemia (AML). Benefit effects of KIR Mismatching was also seen in the cases of Non-Malignant Hematological diseases like Thalassemia. For Thalassemia as the KIR B motif content increases, there is increase in risk of Relapse and not having KIR B motifs content increases the risk of GvHD [11-16].

MATERIALS AND METHODS

This is a study conducted in Nanfang Hospital of Southern Medical University. For this cohort study we took the patients with different hematological malignancies Acute Lymphoblastic Leukemia (ALL) 15, Acute Myeloid Leukemia (AML) 22, Juvenile Myelomonocytic Leukemia(JMML) 23, Lymphoma 1, Chronic Myelogenous Leukemia(CML) 3 and Epstein-Barr Virus(EBV) Infection 1 who underwent HSCT from 2012 to 2018 in our hospital (Table 1). All data were collected from the hospital databases. About 65 patients with different Hematological Malignancies were taken and there HSCT outcome like Overall Survival(OS), Disease Free Survival(DFS), Treatment Related Mortality(TRM), Relapse, Rejection was evaluated on the basis of KIR mismatching. Most of the Patients were followed-up for 5 years. KIR mismatching were done on the basis of model as proposed above and donor Cen B status and KIR B motifs contents were calculated as per mentioned by [10,17].

Table-1: Demographics of the transplanted patients

Variable	Total	Cen B	Non Cen B	B motifs <2	B motifs>2
Median Age, years(range)	6(1-15)	5(1-15)	8(2-13)	8(1-15)	5(1-14)
Gender					
Male	50(76.9)	27(81.8%)	23(71.9%)	34(75.6%)	16(80%)
Female	15(23.1)	6(18.2%)	9(28.1%)	11(24.4%)	4(20%)
Disease					
AML	20(30.8)	7(21.2%)	13(40.6%)	18(40%)	2(10%)
ALL	15(23.1)	7(21.2%)	8(25%)	11(24.4%)	4(20%)
JMML	23(35.4)	17(51.5%)	6(18.8%)	11(24.4%)	12(60%)
others	7(10.8)	2(6.1)	5(15.6%)	5(11.1%)	2(10%)
Disease Status					
CR	24(36.9)	8(24.2%)	16(50%)	22(48.9%)	2(10%)
Non CR	16(24.6)	10(30.3%)	6(18.8%)	9(20%)	7(35%)
Unknown	25(38.5)	15(45.5%)	10(31.2%)	14(31.1%)	11(55%)
Donor					
Haploidentical	18(27.7)	10(30.3%)	8(25%)	12(26.7%)	6(30%)

Variable	Total	Cen B	Non Cen B	B motifs <2	B motifs>2
Non- Haploidentical	47(72.3)	23(69.7%)	24(75%)	33(73.3%)	14(70%)
Donor-Recipient HLA Match					
10/10	1(1.5)	0	1(3.1%)	1(2.2%)	0
9/10	4(6.2)	1(3%)	3(9.4%)	4(8.9%)	0
8/10	11(16.9)	4(12.1%)	7(21.9%)	9(20%)	2(10%)
Less than 8/10	49(75.4)	28(84.8%)	21(65.6%)	31(68.9%)	18(90%)
KIR Mismatch					
Ligand-Ligand					
Match	42(64.6)	19(57.6%)	23(71.9%)	31(68.9%)	11(55%)
Mismatch	22(33.8)	13(39.4%)	9(28.1%)	14(31.1%)	8(40%)
Unknown	1(1.5)	1(3%)	0	0	1(5%)
Receptor-Ligand					
Match	9(13.8)	5(15.2%)	4(12.5%)	7(15.6%)	2(10%)
Mismatch	56(86.2)	28(84.8%)	28(87.5%)	38(84.4%)	18(90%)
KIR Ligands					
C1C1	47(72.3)	23(69.7%)	24(75%)	32(71.1%)	15(75%)
C2C2	1(1.5)	0	1(3.1%)	1(2.2%)	0
C1C2	17(26.2)	10(30.3%)	7(21.9%)	12(26.7%)	5(25%)
DPB1 Status					
Per	30(46.2)	12(36.4%)	18(56.2%)	25(55.6%)	5(25%)
GvH	10(15.4)	7(21.2%)	3(9.4%)	6(13.3%)	4(20%)
HvG	8(12.3)	4(12.1%)	4(12.5%)	7(15.6%)	1(5%)
Unknown	17(26.2)	10(30%)	7(21.9%)	7(15.6%)	10(50%)
GvHD					
aGvHD	10(47.6)	3(37.5%)	7(53.8%)	9(50%)	1(33.3%)
cGvHD	11(52.4)	5(62.5%)	6(46.2%)	9(50%)	2(66.7%)
Graft Type					
PB	36(55.4)	17(51.5%)	19(59.4%)	27(60%)	9(45%)
CB	29(44.6)	16(48.5%)	13(40.6%)	18(40%)	11(55%)

Cen B, Centromeric B; AML, Acute Myeloid Leukemia; ALL, Acute Lymphoblastic Leukemia; JMML, Juvenile Myelomonocytic Leukemia; CR, Complete Remission; KIR, Killer cell immunoglobulin like receptors; Per, Permissible; GvH, Graft versus Host, HvG, Host versus Graft, DPB1, HLA-DPB1; GvHD, Graft versus Host Disease; aGvHD, acute Graft versus Host Disease; cGvHD, chronic Graft versus Host Disease, PB, Peripheral Blood; CB, Cord Blood others diseases like Chronic Myelogenous leukemia, Myelodysplastic Syndrome, Lymphoma, Epstein Barr Virus infection which were included in this data. Unknown, status was unknown.

Cen B motifs and KIR B motifs contents

Comparison was done between Donor with Cen B motifs (having one B motifs in the centromeric part i.e. Cen B/B or Cen A/B) and Donor with Non Cen B motifs (i.e. Cen A/A). Also we compared Donor with High KIR B motifs contents (less than 2 i.e. 0 and 1 or greater than 2 i.e. 2, 3 and 4 KIR B gene motifs) for seeing which better predicted the outcome. Cen B motifs are Cen B1 and Cen B2 and it can be homozygous Cen B i.e. Cen B/B and heterozygous i.e. Cen A/B. Cen A/A contains Homozygous Cen A i.e. Cen A1only. Telomeric part contains Telomeric B motifs i.e. Telomeric B1 and it can be homozygous Tel B i.e. Tel B/B, heterozygous i.e. Telomeric A/B .Telomeric A/A (Tel A/A) as homozygous Telomeric A and its motifs as Tel A1 [7-10].

Statistical Analysis

Four measures of transplant outcome were considered OS, DFS, Relapse, Death (TRM or any others causes of Mortality). (OS and Death) and (DFS and Relapse) were considered as an outcome and predictors as Age, Sex, Donor Cen B Status, Donor B Haplotype Status, Ligand-Ligand Mismatch, Receptor-Ligand Mismatch, Complete Remission(CR) Status, HLA match, Donor KIR B Motifs Content, Donor Tel B Status and Modes of Transplant (Peripheral Blood(PB) or Cord Blood(CB)). OS and DFS were evaluated by the use of Kaplan-Meier curves and other outcomes were evaluated by Pearson Chi-Square test and independent sample T-test. For Pearson Chi-Square test if the expected value were less in the cells Fisher Exact Test was applied. All statistical analysis was done using IBM SPSS Statistics software version 20.

RESULTS

Donor and Recipients Characteristics

For this cohort we took the 65 cases of different Hematological Malignancies that underwent Myeloablative HSCT from 2012 to 2018 in our Hospital. The transplant recipients included patients with early, intermediate, and advanced disease. Only one donor-recipient pairs (AML) was 10/10 HLA-allele matched at HLA-A, B, C, DRB1, and DQB1, and all other had some HLA mismatch. Transplant donors and recipients were typed for presence and absence of individual KIR genes. From the genotypes we determined whether each donor was of A/A or B/x genotype. For the B/x donors we further determined whether their B haplotype genes were in the Centromeric or Telomeric part of the KIR locus, or in both. From these data we calculated the KIR B–content score for each donor, which gives the total number of Centromeric and Telomeric motifs containing B haplotype genes. There was no significant difference in the frequencies of KIR genes, haplotypes, or motifs between either the cohorts of all Hematological Malignancies transplant donors and recipients or with the Asian Chinese population, to which 100% of the donors belonged to. As the Donor were from the Chinese origin from the mainland China and Taiwan. Allogenic Hematopoietic Stem Cell Transplantation was the mode of transplantation in the patients, which included donor with Donor Cord Blood, Peripheral Blood from Matched Related Donor, Matched Unrelated Donor and Haploidentical Donor (Father and Mother).

Table-2: Comparison of outcome of transplanted patients

Predictor		Dead	OS	Statistics	p-value	Relapse	DFS	Statistics	p-value
Age		8.31(3.439)	6(4.103)	t=-2.031	0.047	7.50(3.440)	6.40(4.157)	t=-0.788	0.434
Sex	M F	12(75%) 4(25%)	38(77.6%) 11(22.4%)	X^2=0.044	1	6(60%) 4(40%)	44(80%) 11(20%)	X^2=1.907	0.221
Donor Centromeric Status	Cen B Cen A/A	5(31.2%) 11(61.8%)	28(57.1%) 21(42.9%)	X^2=3.235	0.072	2(20%) 8(80%)	31(56.4%) 24(43.6%)	X^2=4.477	0.044
Donor Telomeric status	Tel B Tel A/A	6(37.5%) 10(62.5%)	25(51%) 24(49%)	X^2=0.884	0.347	3(30%) 7(70%)	28(50.9%) 27(49.1%)	X^2=1.483	0.309
Donor KIR B Content Scores	<2 >2	14(87.5%) 2(12.5%)	31(63.3%) 18(36.7%)	X^2=3.326	0.117	10(100%) 0(0%)	35(63.6%) 20(36.4%)	X^2=5.253	0.025
Donor Haplotype Status	A Haplotype B Haplotype	7(43.8%) 9(56.2%)	12(24.5%) 37(75.5%)	X^2=2.163	0.205	5(50%) 5(50%)	14(25.5%) 41(74.5%)	X^2=2.464	0.141
Ligand-Ligand Mismatch	Match Mismatch	12(75%) 4(25%)	31(65.6%) 17(35.4%)	X^2=0.591	0.442	8(80%) 2(20%)	35(64.8%) 19(35.2%)	X^2=0.883	0.476
Receptor-Ligand Mismatch	Match Mismatch	3(18.8%) 13(81.8%)	6(12.2%) 43(87.8%)	X^2=0.428	0.678	3(30%) 7(70%)	6(66.7%) 49(87.5%)	X^2=2.585	0.135
CR Status	CR Non CR Unknown	6(37.5%) 7(43.8%) 3(18.8%)	18(36.7%) 9(18.4%) 22(44.9%)	X^2=5.303	0.071	3(30%) 5(50%) 2(20%)	21(38.2%) 11(20%) 23(41.8%)	X^2=4.294	0.117
HLA Match	HLA>8/10 HLA<8/10	3(18.8%) 13(81.2%)	13(26.5%) 36(73.5%)	X^2=0.393	0.741	2(20%) 8(80%)	14(25.5%) 41(74.5%)	X^2=0.136	1
Modes of Transplant	PB CB	10(71.4%) 4(28.6%)	26(53.1%) 23(46.9%)	X^2=1.5	0.221	8(80%) 2(20%)	28(52.8%) 25(47.2%)	X^2=2.536	0.167

OS, Overall Survival; DFS, Disease Free Survival; Cen B, Centromeric B motifs; Cen A/A, Centromeic A/A; Tel B, Telomeric B motifs; Tel A/A, Telomeic A/A; PB, Peripheral Blood; CB, Cord Blood; KIR, Killer Immunoglobulin Cell like Receptor; CR, Complete Remission; HLA, Human Leukocyte Antigen Unknown, Status was unknown.

KIR Mismatching

Ligand-Ligand and Receptor-Ligand Mismatch

In the Ligand-Ligand mismatch there were 20 patients mismatched, as for Receptor-Ligand mismatch there were 56 patients with mismatch. Ligand-Ligand model missed out the 36 patients that was mismatched at Receptor-Ligand level. In our study, Receptor-Ligand model predicted the better outcome than Ligand-Ligand model but the results were not significant, may be more data are required to carry on further comparison.

Cen B Motifs Donor has a better HSCT outcome

In our study, we found that selecting the Donor with Cen B motifs predicted the better outcome of HSCT than other model of KIR Mismatch. Even with the small sample size choosing Donor with Cen B gave the better outcome of HSCT. It was found that Cen B motifs donor were superior in HSCT outcome than Non Cen B motifs i.e. Cen A/A donor. We found that Cen B motifs donor had the higher survival and relapse protection for pediatric hematological malignancies（DFS 56.482,95% confidence interval 51.763-61.201, p=0.034） (RR 0.242 ,95% confidence interval 0.056-1.056, p=0.044) (OS 51.437, 95% confidence interval 44.527-58.347, p=0.082) compared to Cen A/A donor (Fig.1). Results for Donor with Tel B motifs was not statistically significant. Even with the small sample size Cen B motifs donor had the better HSCT outcome.

DFS (Disease Free Survival)

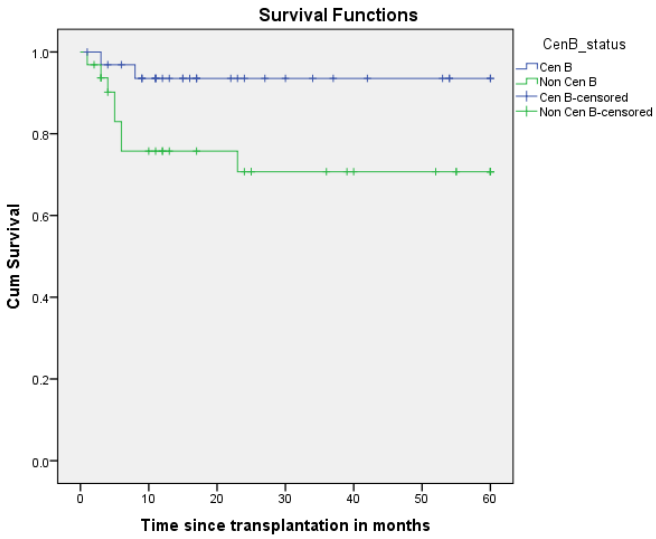

Fig-1: Kaplan-Meier for DFS between Cen B and Non-Cen B

High Donor KIR B gene motifs contents have a better HSCT outcome

In our study, we also found that selecting the donor with High KIR B gene motifs contents had a better HSCT outcome. KIR B motifs contents >2 was superior in HSCT outcome than KIR B motifs contents <2. Donor with greater than two B motifs contents had a better survival outcome and less relapse (DFS p=0.027) (RR 0.778, 95% confidence interval 0.665-0.909, p=0.025) (OS 42.554, 95% confidence interval 34.967-50.142, p=0.087) compared to B motifs contents less than two (Fig.2). KIR B motifs contents >2 did not have any patients with relapse (Table 2).

DFS (Disease Free Survival)

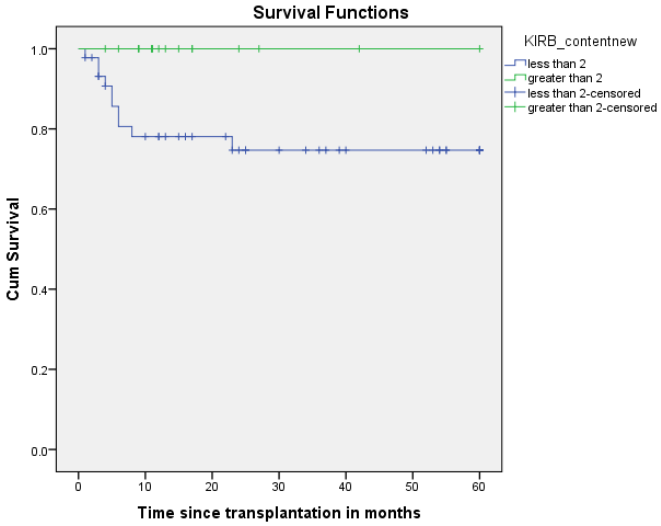

Fig-2: Kaplan-Meier for DFS between B motifs contents greater than 2 and B motifs contents less than 2

Donor KIR B motifs content>2 has less GvHD

Donor KIR B motifs content>2 has less likelihood than donor KIR B motifs content <2 of having GvHD. In our study p value was significant at 0. 047. Donor KIR B motifs contents>2 was a protective factor for GvHD (Table 3).

Table-3: GvHD status of the transplanted patients

Predictor		GvHD	No GvHD	Statistics	p
Age		8.52(3.57)	5.64(3.96)	t =-2.887	0.006
Sex	M F	14(66.7%) 7(33.3%)	36(81.8%) 8(18.2%)	X^2=1.838	0.214
Donor Centromeric Status	Cen B motifs Cen A/A	8(38.1%) 13(61.9%)	25(56.8%) 19(43.2%)	X^2=1.994	0.158
Donor Haplotype Status	A Haplotype B Haplotype	8(38.1%) 13(68.9%)	11(25%) 33(75%)	X^2=1.178	0.278
Donor B motifs contents	<2 >2	18(85.7%) 3(14.3%)	27(61.4%) 17(38.6)	X^2=3.957	0.047
Donor Telomeric Status	Tel B motifs Tel A/A	8(38.1%) 13(61.9%)	23(52.3%) 21(47.7%)	X^2=1.145	0.285
Ligand-ligand mismatch	Match Mismatch	13(61.9%) 8(38.1%)	29(67.4%) 14(32.6%)	X^2=0.192	0.661
Receptor-ligand mismatch	Match Mismatch	1(4.8%) 20(95.2%)	8(18.2%) 36(81.8%)	X^2=2.146	0.251
CR Status	CR Non CR Unknown	15(71.4%) 2(9.5%) 4(19%)	9(20.5%) 14(31.8%) 21(47.7%)	X^2=15.914	0.00
HLA match	HLA>8/10 HLA<8/10	9(42.9%) 12(57.9%)	7(15.9%) 37(84.1%)	X^2=5.563	0.018
Graft type	PB CB	12(57.1%) 9(42.9%)	24(54.5%) 20(45.5%)	X^2=0.039	0.844

GvHD, Graft versus Host Disease; Cen B motifs, Centromeric B motifs; Cen A/A, Centromeric A/A; Tel B motifs, Telomeric B motifs; Tel A/A, Telomeric A/A; PB, Peripheral Blood; CB, Cord Blood; KIR, Killer Immunoglobulin Cell like Receptor; CR, Complete Remission; HLA, Human Leukocyte AntigenUnknown, Status was unknown.

HLA match >8/10 had less GvHD compared to HLA match<8/10 groups

HLA match >8/10 had less GvHD compared to HLA match<8/10 groups as p was significant at 0. 018. Greater the HLA mismatching greater the chances of GvHD, as per Donor selection criteria we need to match Donor-recipient HLA as much as possible. Donor with the match are more preferable over Donor mismatching at different loci of HLA.

DISCUSSION

KIR genotype varies with the population and the country, population of the country also consists of different ethnic groups of different origins. So, there is the possibility of the outcome may vary within country and its population. Mostly in northeast Asians Haplotype A is more commonly seen than haplotype B but in population like India, Australia, America and most of Caucasian populations haplotypes A and B have a more even distribution [18-21]. In Southern Han population of China, the ratio of haplotype A vs. B is about 3:1 (74.8% vs. 25.2%) [22], which is similar to previous studies conducted in Han populations from Zhejiang and Taiwan [23]. Many of the studies that were conducted for KIR mismatching for HSCT outcome includes the Caucasian group of population where Haplotype B is more commonly seen or Haplotype A or Haplotype B is evenly distributed, as this was the study conducted in Chinese population where Haplotype A is commonly seen, there is some possibility that outcome may vary. Some of the study done in this part of the world has shown some beneficial as well as detrimental effects of KIR mismatching. Results may vary according to materials and methods that were used like KIR mismatching model, regimens used, mode of transplants, methods of donor selection, severity of the disease, etc. Some of the study that were conducted in this part of the world on the basis of KIR Mismatching in the recent years are as follows: transplant from donors carrying Cen-B was associated with an increased survival compared with Cen-A homozygous donors [24], Haplotype Bx showed higher overall survival rate [25], missing ligand for the donor inhibitory KIR has weak effect on the outcome of unmanipulated HSCT and activating KIR play an important role in the EFS, relapse and TRM after HSCT [26], Incidence of grade II-IV acute graft-versus-host disease (aGVHD) was significantly lower in patients of KIR/HLA matched group than in KIR/HLA mismatched group [27], KIR ligand mismatch is a poor prognosis factor for the patients with HLA

mismatched HSCT, and is a useful parameter for donor selection[28]. KIR could impact outcome and donor KIR haplotype with Cen-B confer significant survival benefits to HLA-identical sibling HSCT [29]. Not many researches and study could be found about KIR Mismatching in Chinese Asian Population so there is a much need for more researches and more study to be conducted in this part of the world in order to know how much the region, geography and population affect the HSCT outcome by KIR mismatching.

KIR studies and researches have been around us for more than two decades still there are many questions that needs to be answers, so knowing more about their gene repertoires, knowing more about their effect on corresponding ligands will open wide range of possibility in the field of HSCT. Many researches are going on and many questions are being answered, many things that were thought to be impossible are seemingly possible now. Although it has been recognized that NK cells exhibit enhanced antineoplastic activity in HLA-mismatched HSCT environments, the benefits of donor selection based on KIR genotyping have not been well established, and many studies are continuing. Many institutions have established local guidelines to help select donors with HLA and KIR genotype mismatching for NK cell alloreactivity; however, the definitions and models used by these centers are not standardized, which highlights the importance of well-designed prospective donor selection studies. NK cells and KIR immunogenetics may play an increasingly important role in selecting the best donor for transplantation with HLA matching, CMV status, blood type, age, parity and gender. In addition, determining the best donor based on KIR genotype may be an important next step in designing successful NK-based interventions. The more research that come out from around the world, there is greater the likelihood of acceptance and practice.

CONCLUSION

We could conclude that the best strategy to increase better HSCT outcome is to select the donor with Cen B motifs and donor with KIR B gene motifs contents >2. In our study, we also found that Donor with KIR B motifs contents had less GVHD compared to donor KIR B motifs content <2; also HLA match >8/10 had less GvHD compared to HLA match <8/10. Even with small sample size, these predictors predicted the outcome of HSCT better than any other model. There is increased likelihood of survival just by selecting Donor on the basis of Cen B motifs status and High KIR B gene motifs contents. In our study they were the predictors who influenced the outcome even in the small sample size relative to other KIR Mismatching model.

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