VOLUME-7, ISSUE-2, FEBRUARY-2018 • PRINT ISSN No 2277 - 8160

Original Research Paper

Medical Science

FETOMATERNAL OUTCOME IN SICKLE CELL HEMOGLOBINOPATHY

Dr Tushar Jyoti Kar	Professor & HOD , Department of Obstetrics And Gynaecology VSSIMSAR Burla , Odisha
Dr Lina Baru*	Assistant professor , Department of, Obstetrics And Gynaecology, VSSIMSAR Burla , Odisha *Corresponding Author
Dr Ganeshram Bhoi	Postgraduate Department of Obstetrics and Gynaecology, VSSIMSAR Burla, Odisha
Dr Ranjita Patnaik	Senior resident Department of Obstetrics and Gynaecology, VSSIMSAR Burla, Odisha

ABSTRACT

Background- Ours is a tertiary care hospital with a catchment area of Odisha & part of Chattishgarh has high prevalence of sickle cell hemoglobinopathy .

Method- A prospective case control study of two years duration with sample comprised of 2040 pregnant women attending O&G OPD & LR .

Result- Out of 2040 women 98(4.8%) had sickle cell hemoglobinopathy, with sickle cell disease SS(n=32) 1.56% & sickle cell trait AS(n=66) 3.23%.There was increased risk of complications in women with (SS) like crisis(25%), PIH (28.1%) ,anemia (100%) ,UTI (31.25%) ,PPH (25%) ,IUGR (18.8%), need of blood transfusion (40.6%), maternal mortality (12.5%) , LBW (65.5%), low apgar score (17.9%) & NICU admissions(28.57%) respectively as compared to women with (AS) where crisis (3%) , PIH (6%) ,anemia (95.5%),UTI(19.7%) ,PPH (9.5%) ,IUGR (7.6%), need of blood transfusion (6.1%), no maternal mortality , LBW (28.8%),low apgar score (3%) and NICU admissions(10.6%) respectively.

Conclusion- The rate of complication is high in SS case. Screening and early, aggressive and comprehensive Antenatal & perinatal care can improve fetomaternal outcome.

KEYWORDS : Sickle cell hemoglobinopathy,fetomaternal outcome.

Introduction –

Hemoglobinopathy are diverse group of inherited disorders of hemoglobin production and function , comprises a group of diseases characterized by the presence of sickle hemoglobin (Hb S). It is classified as sickle cell disease (Hb SS), sickle cell trait(Hb AS), Sickle-beta thalassemia (Hb S-beta) and other associations of mutant hemoglobins with Hb S.

In low oxygen tension, HbS solubility decreases, resulting in the polymerization of these molecules affects the red cell structure, changing it into a sickle-shaped, damaging the cell membrane, making it more rigid and exposing a greater number of adhesion molecules on the cell surface, increases the adherence of red cells to the vascular endothelium which is named as sickling that causes vessel occlusion , tissue ischemia and painful crises in this disease. Chronic haemolytic anemia and frequent vaso-occlusive crises cause damage to various organs . Until the 1970s, the management of sickle cell patients was poor and pregnancy was associated with high maternal and fetal mortality. With newborn screening and preventive measures such as vaccination and antibiotic prophylaxis since birth, patient survival has improved. 50%–70% of pregnant women with SCD require at least one hospitalization and 30%–40% require transfusion. 20%to50% of SCD Women with previous frequent transfusion are alloimmunized and Pulmonary hypertension affects 6%–11% . SCD are more prone for preeclampsia and eclampsia, VTE , infections (UTI, pneumonia, sepsis and postpartum infections), acute renal failure ,death and there is increased risk of fetal growth restriction, preterm delivery, and stillbirth.Sickle cell disease in Odisha having high prevalence in western part (10-15%) in the general population. Predominantly confined to certain group of population (i.e. Agharias, Kulta, Schedule caste and schedule tribe) and also reported in many upper caste of Hindus (Kar et al 1987).

Objectives of the study:

To asses & compare fetomaternal outcomes in sickle cell hemoglobinopathies(SS&AS) .

METHODS-

With due permission of hospital ethical committee and after obtaining the consent from the patient a prospective case control study was conducted in our hospital from 2015 to 2017 .

Inclusion Criteria-

Pregnant women attending O&G OPD and labour room for safe confinement .

Exclusion Criteria-

1. Pregnant women with pre-existing medical disease like Herat disease, Dibetes Mellitus, Hypertension, Renal disorders and other chronic illness.
2. Rh negative pregnancy.

Out of 2040 pregnant women 98 were found to have sickle cell anaemia and evaluated with Hb electrophoresis at our sickle cell unit . Of which 32 had SCD and 66 had SCT. Cases were matched for age ,socioeconomic status with control group who were negative for sickling test and without risk factors like heart disease, diabetes mellitus, hypertension, Rh negative and studied for comparison. Patient information entered on a predesigned proforma. .General, systemic and obstetric examinations done at the time of admission. Obstetrics history, antenatal complications, history of blood transfusion,sickle cell crisis, mode of delivery were noted. In all cases Haemoglobin estimation and Urine microscopic to detect RBC and pus cell was done. Ultrasound examination were done in all cases that presented in antenatal period. According to the standard hospital protocol all patients were managed. Blood transfusion were carried out for patients with haemoglobin less than 6 gram%. Mode of delivery, indications of caesarean section, maternal complications were noted. Foetal outcome like live born or still born, birth weight, babies requiring NICU care were noted.All Information were tabulated in Microsoft excel sheet. Statistical analysis carried out in SPSS 17 .

RESULTS :

The Feto-Maternal outcome of pregnancy was studied in the patients of SCD & SCT which were compared with control group.

TABLE – 1: PREVALENCE OF SICKLE CELL DISEASE AND SICKLE CELL TRAIT

CATEGORY	NO.OF CASES	PERCENTAGE(%)	PREVALENCE PER THOUSAND
SS	32	1.56	15.6
AS	66	3.23	32.3
CONTROL	1942	95.19	951.9
TOTAL	2040	100	100

Sickle cell hemoglobinopathy was found in 98 cases (4.8%), out of which SS 32 (1.56%) and AS 66(3.23%).

TABLE -2 :DISTRIBUTION OF PREGNANT MOTHERS ACCORDING TO AGE

AGE (YEAR)	SS(32)		AS(66)		CONTROL(98)	
	NO.	%	NO.	%	NO.	%
<20	6	18.75	7	10.6	13	13.3
20-30	26	81.25	59	89.39	83	84.7
>30	0	0	0	0	2	2.04
Mean age	23.5		24.2		24.23	

Mean age of the pregnant mothers with SS, AS and Control group were 23.5, 24.2 and 24.23yrs respectively . Majority of SS are multipara(56.25%) while(43.8%) are nullipara.

TABLE -3: HEMOGLOBIN CONCENTRATION IN CASE OF PREGNANT MOTHERS

Hb GM%	SS		AS		CONTROL	
	NO	%	NO.	%	NO.	%
≤ 6	13	40.6	4	6.1	4	4.1
6.1-9	13	40.6	32	48.5	32	32.7
9.1-11	6	18.8	27	40.9	54	55.1
>11	0	0	3	4.5	8	8.2
MEAN Hb	7.65		9.22		9.52	

Taking normal haemoglobin concentration as 11gm% , 100% of SS mothers, 95.5% of AS mother, 91.9% of mothers of control group were found to be anaemic. Peripheral smear examination and red cell Indices revealed that the anaemia was normocytic normochromic .40.6%,6.1% and 4.1% of women in SS, AS and Control group respectively were severely anaemic. The mean haemoglobin level of SS mothers were significantly low compared to Control mother (p value = 0.000).

TABLE -4:MATERNAL COMPLICATION IN CASE OF SS, AS & CONTROL GROUP

COMPLICATION	SS(32)		AS(66)		CONTROL(98)	
	NO.	%	NO.	%	NO.	%
CRISIS	8	25	2	3	0	0
PIH	9	28.1	4	6	6	6.1
PPH	8	25	6	9.1	9	9.2
IUGR	6	18.8	5	7.6	8	8.2
BT	13	40.6	4	6.1	6	6.1
MORTALITY	4	12.5	0	0	0	0
UTI(pus cell>5)	10	31.25	13	19.7	11	11.22
PRETERM<37 weeks	13	40.6	14	21.2	16	16.3
TERM>37weeks	19	59.4	52	78.8	82	83.7

Painful crisis was seen in 25% of case of SS group. Incidence of PIH & PPH were high in case of SS group 28.1% & 25% as compare to 6.1% & 9.2% respectively in Control group which were statistically significant with p value = 0.001 and 0.039 respectively. IUGR found in 6(18.8%), 5(7.6%) & 8(8.2%) in SS, AS, and Control groups respectively with no significant difference of incidence between study and control group.

Blood transfusion required in13(40.6%),4 (6.1%) & 6(6.1%) cases of SS, AS, and Control mothers respectively .The need of blood transfusion was higher in case of SS in compare to Control group (p value =0.000).

Maternal mortality is seen in 4(12.5%) cases of SS mother. No maternal death found in case of AS and Control mother. Urinary tract infection is highly seen in case of SS group compare to Control with a significant p value of 0.028.UTI in case of AS group were comparable to Control group.

Incidence of preterm labour was 40.6% in SS group compare to Control which is statistically significant (p value = 0.015).

TABLE 5:MODE OF DELIVERY IN CASE OF SS, AS & CONTROL GROUP

MODE OF DELIVERY	SS(32)		AS(66)		CONTROL(98)	
	NO.	%	NO.	%	NO.	%
VD	15	46.9	36	54.6	50	51.02
INSRUMENTAL	2	6.3	3	4.5	6	6.1
LSCS	15	46.9	27	40.9	42	42.9

Vaginal delivery was in 15(46.9%), 36 (54.6%),50(51.02%) of SS, AS ,and Control mother respectively.Instrumental delivery was in 2(6.3%),3(4.5%),and 6(6.1%) of SS ,AS and Control mother respectively,however LSCS were 15(46.9%),27(40.9%),42(42.9%) respectively.Fetal distress was the most common indication followed by IUGR in SS group.

TABLE -6 : NEONATAL OUTCOME IN CASE OF SS, AS &CONTROL MOTHERS

FETAL OUTCOME	SS(32)		AS(66)		CONTROL(98)	
	NO.	%	NO.	%	NO.	%
LB	28	87.5	66	100	93	94.9
SB	4	12.5	0	0	5	5.1

The incidence of still birth in SS mothers (12.5%) is high compare to Control with a statistically significant P value of 0.02.

TABLE-7:NEONATAL COMPLICATIONS IN CASE OF SS, AS, CONTROL GROUP

COMPLICATIONS	SS(28)		AS(66)		CONTROL (93)	
	NO.	%	NO.	%	NO.	%
HIE	5	17.85	4	6.06	4	4.3
SEPTICEMIA	3	10.71	2	3.03	3	3.22
ANEMIA	4	14.28	1	1.51	1	1.07
JAUNDICE	7	25	5	7.57	5	5.37
APGAR SCORE<4	5	17.9	2	3	0	0
LOWBIRTH WEIGHT<2.5 kg	21	65.6	19	28.8	24	24.5
NICU ADMISSION	8	28.57	7	10.6	9	9.67
PERINATAL DEATH	8	25	3	4.5	9	9.18

HIE was found more in17.85% case of babies born to SS mothers more compare to Control with significant p value of 0.044.Incidence of HIE in AS (6.06%) were comparable to Control (4.3%).Neonatal septicaemia was seen in 3(10.71%),2 (3.03%),3(3.22%) of babies of SS, AS and Control group respectively. More cases of anaemic babies were found in case of SS (14.28%) compare to Control(1.07%) with statistically significant p value of 0.001.AS group and Control group are comparable in terms of anaemic babies. It was observed that jaundice was present in more numbers of babies born to SS (25%) compare to Control(5.37%) with a significant p value of 0.006. 17.9% babies born to SS mothers had Apgar score(<4) at 5 minutes,which was more compared to control group (p value =0.001).Low birth weight babies were observed more in SS group(65.6%) compare to control (p value = 0.000). There is no significant difference in the incidence of low birth weight babies in between AS and Control group The rate of admission in SNCU was statistically significant in case of babies born to SS(28.57%) compare to Control (p value = 0.026),however it was 10.6% in AS comparable to Control (9.67%).The higher incidence of Perinatal deaths was statistically significant in case of babies of SS mother(25%) compare to Control (p value =0.007).

DISCUSSION:

The prevalence of sickle cell hemoglobinopathy in general

population of western Odisha as reported by Kar(1986) is15.1%.As the women of reproductive age group in the general population constitute approximately 25%, the sickle cell gene frequency is expected to be 3.75%. Higher incidence (4.8%) in this study is because our institute got referral cases from western Odisha and some part of Chhattisgarh. Study by Adam et al (1953) and Mc Curdy series (1964) the prevalence of SCT was 79/1000 and 64/1000 respectively.The prevalence of SCT in the present study is 32.3/1000 low due to small sample size.

The mean age of pregnant mothers with SS, AS, and Control group were 23.5, 24.2, 24.23 respectively corresponds closely to the study by Anderson et al.(1949).

In the present the mean haemoglobin concentration in SS ,AS and conrol group were 7.65gm%,9.22gm% and9.52gm% respectively similar to that of Tuck et al(1983) who observed that 65% of SS mother in UK had haemoglobin concentration of less than 10gm%.Sonwane Anju S.et al(2005) also found the mean haemoglobin as 7.65gm% in SS mothers,8.77gm% in AS mothersThe causes of anaemia in these women are continued hemolysis,sequestration crisis,iron and folate deficiency.Due to qualitative defect in haemoglobin they are more prone for destruction resulting in anaemia with increased incidence of blood transfusion and iron overload. RCOG doesn't advice the use of prophylactic blood transfusion during pregnancy. In present study (40.6%) SS required blood transfusion during pregnancy which is significantly high compare to AS group(6.1%) and Control group(6.1%). Mayur.M.,Daigavane et al(2013),and Resende et al(2014) reported 46.6%,and 51.9% of patients required blood transfusion during pregnancy. In our institution we have kept a maintenance level of 9gm%. So we discourage prophylactic blood transfusion when haemoglobin level more than 9gm%.

The incidence of urinary tract infection in present study was 31.25% in SS women,19.7% in AS women was significantly high compared (p value-0.028) to Control group (11.22%).This finding is in accordance with authors like Mc Curdy et al(1946) and Tuck et al(1983) may be due decrease resistant due to low immunity and severe anaemia.

Present study corresponds to the study by Afolabi BB et al(2009) and Serjeant GR(2004) et al who observed there is no significant difference of incidence of preeclampsia between SCD mother and Control mothers.

The painful crisis(25%) in SS is high is due to haemolytic crisis and anaemia.coresponding to studies done by Oteng-Ntim et al(2015),Mayur M.,Daigavane et al(2013),Al Kahtani(2012) and Alayed et al(2014).

In the present study out of 4 (12.5%) maternal death in case of SS mother is highly significant compare to AS and Control .out of this mortality 50% were associated with comorbid condition like eclampsia. Other 50% were suffered from painful crisis and acute chest syndrome. similar pulmonary complications observed in studies by Dai vagane et al(2013)(10%) and Resende et al (2014)(29.6%)Wide variation in mortality rate among different parts of world is due to unavailability of proper heath care facility in developing country.

Incidence of PPH in SS women was significantly high Kobak et al reported similar observations in SS women..More PPH are due to anaemia and toxaemia of pregnancy.

Desai G et al(2017) found increase incidence of preterm delivery in SCD mother compare to control comparable to present study . Sonwane Anju S et al (2005) found preterm deliveries of 30.10% in AS more than present study(21.1%) that may be due to small sample size.

Pregnant women with SCD without complications should be delivered around 38-40weeks[Can Boga et al(2016)] . Caesarean section should be done for obstetrical conditions only. [(Howard J et al)(2012] High incidence of caesarean section in SS in the present study(46.9%) comparable to study by Alayed et al(2014)(36%) and Boulet et al (2013)(43%) may be due to increased maternal and foetal complications during pregnancy .

12.5% babies of SS mothers were stillborn as compare to 5.1% in case of control mother which is significantly high with a p value of 0.02.In present study it was found that in case of AS group 100% babies were live born. Fort et al(1971) reported that the perinatal mortality(still born +early neonatal death) in SS mothers was around 30% comparable to the present study perinatal death 25% whereas perinatal death of Control group was 9.18% .However Hendrickse et al from Nigeria reported that the perinatal mortality rate in pregnant SS mother was not significantly high in patients who receive accessible care throughout pregnancy.

Tuck et al(1983),Tita et al(2007)found no increase in the risk of stillbirth in women with SCT when compared with those with normal haemoglobin.In present study the perinatal death in case of AS group was 4.5% lower than control which may be due to small sample size.

High incidence 65.6% of low birth weight in SCD mothers in this study as compared to53% reported by Daigavane ,Kar T J (2013) and 32.4% by Al-Farsi et al(2014) .High incidence of low birth weight due to fetal hypoxia throughout the pregnancy caused by anaemia and fetoplacental insufficiency,low socioeconomic status and inadequately supervised pregnancy.Whereas in AS (28.8%) which was comparable to Control (24.5%) with no statistical significant difference which corresponds to the studies by Blattner P et al (1977) .There was significantly high rate of admission to SNCU 28.57% of babies of SS group is comparable to 23.33% by Daigavane,MM ,Jena R.K ,Kar T J(2013) .Neonatal septicaemia,fetal anemia and jaundice, significantly high in SS group due to increase incidence of chronic hypoxia,anaemia,sickle cell crisis,vasculopathy and preterm delivery.

CONCLUSION-

Sickle cell hemoglobinopathy encounter more complications than general population. The complications are maximum in SCD. Our study shows a close monitoring of individual pregnancy with SCD and SCT can result in good feto maternal outcome. A multidisciplinary approach is required for comprehensive management so that complications to be dealt with appropriately. Premarital counselling and testing for the sickle cell gene, identification of antenatal complications, and good intra natal management in a well equipped hospital will help in achieving the improvement of foetalmaternal outcomes . There is a need for screening programme of this disease in all neonates of western Odisha belt.

DECLARATIONS

Funding: none

Conflict of interest: none

Ethical approval: done by institutional ethical committee

REFERENCE

1) Afolabi BB.,IwualaNC.,Iwuala IC. & Ogedengbe OK. Morbidity and mortality insickle cell pregnancies in Lagos, Nigeria: A case control study. Journal of Obstetricsand Gynaecology, 2009; 29(2): 104–106
2) Al-Farsi, S.H., Al-Khabori, M.K., Al-Hunieni, M.N., Al-Riyami, N.M.,Fetaloutcomes in pregnant women with sickle cell disease. Saudi Med. J. 2014;5(35):472–476.
3) Al Jama FE, Gasem T, Burshaid S, Rahman J, Al Suleiman SA, Rahman MS. Pregnancy outcome in patients with homozygous sickle cell disease in a university hospital, Eastern Saudi Arabia. Arch Gynecol Obstet. 2009;280:793–797.
4) Al Kahtani, M.A., AlQahtani, M., Alshebaily, M.M., Abd, E., Izaher, M., Moawad,A.,Aliohani, N.,. Morbidity and pregnancy outcomes associated with sicklecellanemia among Saudi women. Int. J. Gynaecol. Obstet. 2012;119:224–226.2005;112(9):1308-1314
5) Alayed N, Kezouh A, Oddy L, Abenhaim HA. Sickle cell disease and pregnancy outcomes: population-based study on 8.8 million births. J Perinat Med. 2014;42:487–492..
6) Anderson GW et al-Sickle cell anemia and pregnancy.Am j Obstet Gynecol,1949; 58:75-89

7) Barfield WD, Barradas DT, Manning SE, Kotelchuck M, Shapiro-Mendoza CK. Sickle cell disease and pregnancy outcomes: women of African descent. Am J Prev Med. 2010;38:S542–549.
8) Blattner P, Dar H, Nitowsky HM. Pregnancy outcome in women with sickle cell trait.Journal of American Medical Association 1977; 238:1392 – 1394
9) Boulet SL, Okoroh EM, Azonobi I, Grant A, Craig Hooper W. Sickle cell disease in pregnancy: maternal complications in a Medicaid-enrolled population. Matern Child Health J. 2013;17:200–207.
10) Can Boga, HakanOzdoguBaskent.Pregnancy and sickle cell disease :A Reiview of current literature.Critical Reviews in Oncology/Hematology 2016;98:364-374
11) Costa VM, Viana MB, Aguiar RA. Pregnancy in patients with sickle cell disease: maternal and perinatal outcomes. J MaternFetal Neonatal Med ISO. 2014:1–5.
12) Daigavane,M.M, Kar T J, Jena R K . Perinatal outcome in sickle cell disease-Randomized controlled study, Hemoglobin journal, vol. -6, 2013.
13) Desai .G.,Shah .P. et al .Sickle cell disease and pregnancy :A study of community-based hospital in a tribal block of Gujrat ,India,Journalof Health,Population and nutrition,2017;36.3,DOI 10.1186
14) D.R. Powars, M. Sandhu, J. Niland-Weiss, C. Johnson, S. Bruce, P.R. Manning Pregnancy in sickle cell disease ObstetGynecol, 67 (2) (1986), pp. 217–228
15) Fort A.T et al.counselling the patient with sickle cell disease about reproduction ,Am.J.Obstet .Gynecol 1971;111:324-327
16) Howard RJ, Tuck SM, Pearson TC. Pregnancy in sickle cell disease in the UK: results of a multicentre survey of the effect of prophylactic blood transfusion on maternal and fetal outcome. BJOG. 1995;102:947–951.
17) Kar, B.C., et al. 1986. Sickle cell disease in Orissa State, India. Lancet. 2:1198–1201.
18) Klings ES, Machado RF, Barst RJ, et al. An official American Thoracic Society clinical practice guideline: diagnosis, risk stratification, and management of pulmonary hypertension of sickle cell disease. Am J RespirCrit Care Med. 2014;189:727–740.
19) Mc Curdy PR :Abnormal haemoglobin and pregnancy.Am J ObstetGynecol, 1964; 90:891
20) M.H. Steinberg.Pathophysiology of sickle cell disease.BaillieresClinHaematol, 11 (1) (1998), pp. 163–184.Article | PDF (1779 K) | View Record in Scopus | Citing articles (34)
21) Muganyizi PS, Kidanto H. Sickle cell disease in pregnancy: trend and pregnancy outcomes at a tertiary hospital in Tanzania. PloS one. 2013;8:e56541.
22) Ngo C, Kayem G, Habibi A, et al. Pregnancy in sickle cell disease: maternal and fetal outcomes in a population receiving prophylactic partial exchange transfusions. Eur J ObstetGnecolReprod Biol. 2010;152:138–142.
23) O.S. Platt 1, D.J. Brambilla, W.F. Rosse, P.F. Milner, O. Castro, M.H. Steinberg, et al..Mortality in sickle cell disease. Life expectancy and risk factors for early death N Engl J Med, 330 (23) (1994), pp. 1639–1644 View Record in Scopus | Full Text via CrossRef | Citing articles (1413)
24) Oteng-Ntim, E., Ayensah, B., Knight, M., Howard, J., Pregnancy outcome inpatientswith sickle cell disease in the UK— a national cohort study comparingsickle cellanemia (HbSS) with HbSCdiasease. Br. J. Haematol. 2015a;169(1):129–137.
25) Oteng-Ntim, E., Meeks, D., Seed, P.T., Webster, L., Howard, J., Doyle, P.,Chappel,L.C. Adverse maternal and perinatal outcomes in pregnant womenwith sicklecell disease: systematic review and meta-analysis. Blood 2015b;125(21):3316–3325.
26) Resende Cardoso, P.S., Lopes Pessoa de Aquiar, R.A., Vianaa, M.B., 2014. Clinicalcomplications in pregnant women with sickle cell disease: prospective study offactors predicting maternal death or near miss. Rev. Bras. Hematol.Hemoter.2014;36(4):256–263.
27) Serjeant GR, Loy LL, Crowther M, Hambleton IR, Thame M. Outcome of pregnancy in homozygous sickle cell disease. Obstet Gynecol. 2004;103:1278–1285.
28) S.K. Ballas Sickle cell disease: clinical management BaillieresClinHaematol, 11 (1) (1998), pp. 185–214 Article | PDF (4294 K) | View Record in Scopus | Citing articles (34)
29) SonwaneAnuj,pregnancy outcome in women with sickle cell disease and trait. J.of obste.gynecol.2005;55:415-418.
30) Thame MM, Osmond C, Serjeant GR. Fetal growth in women with homozygous sickle cell disease: an observational study. Eur J ObstetGnecolReprod Biol. 2013;170:62–66.
31) Tita TNA, Biggio RJ, Chapman V et al. Perinatal and Maternal Outcomes in WomenWith Sickle or Hemoglobin C Trait ObstetGynecol 2007;
32) Tuck SM, Studd JWW, White JM. Pregnancy in women with sickle cell trait.BritishJournal of Obstetrics and Gynaecology 1983; 90:112 – 117.
33) Villers MS, Jamison MG, De Castro LM, James AH. Morbidity associated with sickle cell disease in pregnancy. Am J Obstet Gynecol. 2008;199:125 e121–125.
34) Yazdanbakhsh K, Ware RE, Noizat-Pirenne F. Red blood cell alloimmunization in sickle cell disease: pathophysiology, risk factors, and transfusion management. Blood. 2012;120:528–537.
35) Yu CK, Stasiowska E, Stephens A, Awogbade M, Davies A. Outcome of pregnancy in sickle cell disease patients attending a combined obstetric and haematology clinic. J ObstetGynaecol. 2009;29:512–516.