Influence of Sickle Cell Trait on Pregnancy Outcome

Authors

Dr Neha Nimbark

MS OBGY,

Associate professor of Department of Obstretics and Gynaecology, ,

Dhiraj Hospital and SBKS medical institute and research centre,

Sumandeep Vidyapeeth, Pipariya

Taluka Waghodia, Dist Vadodara, Gujarat 391760

Dr Deep Diora

2nd year resident in Department of Obstretics and Gynaecology,

Dhiraj Hospital and SBKS medical institute and research centre,

Sumandeep Vidyapeeth, Pipariya

Taluka Waghodia, Dist Vadodara, Gujarat 391760

Dr Prachi Kothari

2nd year resident in Department of Obstretics and Gynaecology,

Dhiraj Hospital and SBKS medical institute and research centre,

Sumandeep Vidyapeeth, Pipariya

Taluka Waghodia, Dist Vadodara, Gujarat 391760

Abstract

Background :SCT results from inheritance of one gene for haemoglobin S and one for normal haemoglobin A. The heterozygous inheritance of the gene for haemoglobin S results in sickle cell trait or AS haemoglobin. Hb A is most abundant and the amount of haemoglobin S averages only approximately 30% in each red cell. Individuals who are heterozygous for Hb S are carriers of the sickle cell trait (SCT).

Methods :A retrospective randomised comparative study of pregnancy outcome in sickle cell trait vs sickle negative patients. Total sample size taken 150. Patients are compared in regard with antenatal , intrapartum and post natal complications.

Results :SCT, 45%. Of the patients had mild andmoderateanaemia. Severeanaemia(8%)received Blood Transfusion. Mostly the patients had preterm delivery 47%. Mode of delivery included most commonly vaginal delivery 60%.Most of the new born were low birth weight 49%.Most common post-partum complication included fever in case group 16%. It was found that 12% of the Spouse were sickling positiveinSCTgroup.

Conclusions : Sickle Cell Trait is considered a benign state.TheSickleCellTraitpatientsshouldundergoANCregistrationasearlyaspossibleandshouldgoforinstitutional deliveries with NICU and blood bank facility. It should be aimed to avert, detect& abort all possible complications, during this period, toobtainthebestpossiblematernal&perinataloutcome.

Keywords : Sickle Cell Trait, Hemoglobin S, Haemoglobin A, Heterozygous, Preterm Deliveries,

Multi-Disciplinary Approach.

SCT results from inheritance of one gene for haemoglobin S and one for normal haemoglobin A. The heterozygous inheritance of the gene for haemoglobin S results in sickle cell trait or AS haemoglobin. Hb A is most abundant and the amount of haemoglobin S averages only approximately 30% in each red cell. Individuals who are heterozygous for Hb S are carriers of the sickle cell trait (SCT). Heterozygous individuals are generally not anaemic and have normal red blood indices with haemoglobin S percentages near 40%. But under stressful situation these may undergo sickling due to reduced life span of RBC's. They generally enjoy normal life spans. However, there are evidences that carriers have occasional haematuria, renal papillary necrosis, and hyposthenuria. However, women with sickle cell trait are not at great risk for abnormal reproductive course. So, in this study pregnancy outcome in SCT patients is compared with normal patients. This retrospective study was carried out at Dhiraj General Hospital for last one year.

Source of Data:

All patients who were sickling positive were included under this study and the pregnancy outcome

Keywords:

Sickle Cell Trait, Hemoglobin S, Haemoglobin A, Heterozygous, Preterm Deliveries, Multi-Disciplinary Approach

Introduction

The core of the antenatal care programs was developed in the early 20thcentury. The pre- defined screening of pregnant women by a series of examinations &tests at different stages of gestation was designed to detect conditions that threatened the pregnancy. This is known as risk approach.Test for

detection of Sickle cell being one of them.The current knowledge of sickle cell trait in pregnant women is not well understood. Exploring factors that may impact individuals' knowledge of sickle cell trait,will help improve the focus of genetic counselling and assist health care professionals in educating the patients.

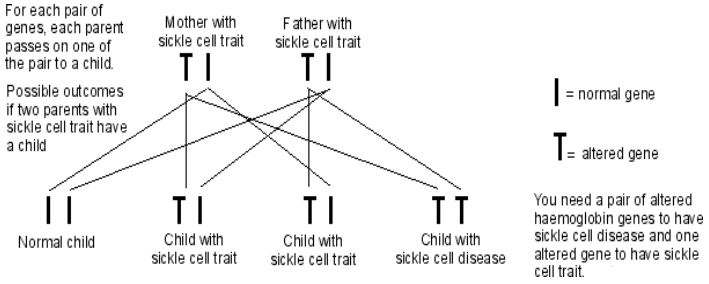
Sickle Cell Anaemia

Sickle cell anaemia include both sickle cell disease and sickle cell trait. The first one is homozygous form with SS genotype whereas the latter on is heterozygous form Ss. In this both MCV and MCHC is reduced. Due to the presence of Hb S these patients are subjected to chronic hypoxia. Sickle cell trait is minor form of Sickle cell anaemia. This is similar to Thalassemia minor. There are more chances of Sickle cell disease patients to land into crisis during an acute episode of physical exertion, dehydration etc. However, in SCT patients crisis can occur if the foetus and mother both are SCT. Thus, it is recommended to supplement the patients with SCT with hydroxyurea in $2^{nd}/3^{rd}$trimester of pregnancy to prevent intrapartum and postpartum complications.[1]

Sickle Cell Trait

It results from inheritance of one gene for haemoglobin S and one for normal haemoglobin A. The heterozygous inheritance of the gene for haemoglobin S results in sickle cell trait or AS haemoglobin. Hb A is most abundant and the amount of haemoglobin S averages only approximately 30% in each red cell.[2]

Acquiring sickle cell trait:



Health Concerns of individuals with SCT

Traditionally, sickle cell trait has been viewed as benign condition, non-disease, partially protective against falciparum malaria and without any painful episodes characteristic of the homozygous sickle cell disease. On population basis, sickle cell trait has no discernible impact on life expectancy. Individuals who are heterozygous for Hb S are carriers of the sickle cell trait (SCT). Heterozygous individuals are not anaemic and have normal red blood indices with haemoglobin S percentages near 40%.[2] They generally enjoy normal life spans without serious health consequences related to their sickle cell status, but under extreme conditions such as severe dehydration and high intensity physical activity, complications such as exertional rhabdomyolysis, splenic infarction, and renal papillary necrosis can occur.[3] Sickle cell trait occurs in approximately 300 million people worldwide, with the highest prevalence of approximately 30 to 40% in sub-Saharan Africa [4] . In regions, of the

world where malaria is endemic, SCT confers a survival advantage in childhood malaria, this was thought to be a major selective pressure for persistence of the Hb S mutation (Glu6Val). There are evidences that carriers have occasional haematuria, renal papillary necrosis, andhyposthenuria[4]However, women with sickle cell trait are not at great risk for abnormal reproductive course.

Pre-conceptional counselling

One important problem sickle cell trait is the possibility of transmission of the abnormal gene to their discordant. Women with sickle cell trait should have pre-conceptional counselling and the male partner should be examined to determine whether or not he also carries the trait. In case, the father is a carrier there is 25% chance that the infant will be homozygous and will be sickle cell disease. In this situation, early prenatal diagnosis is important because it will allow the possibility of pregnancy termination. Early pre-natal diagnosis is possible with the use of polymerase chain reaction (PCR).

Influence on Pregnancy & Labour

Adequate management of pregnant women with sickle cell hemoglobinopathies requires close observation. These women maintain haemoglobin mass by intense hemopoiesis in order to compensate for the markedly shortened RBC's life span. Prenatal folic acid supplementation with 4mg/day is needed to support the rapid turnover of red blood cells[5]. Assessment of fetal health is also important as it may lead to fetal growth restriction and perinatal morbidity. A series of serial sonography and antenatal fetal surveillance should be carried out.

Aims

- To study maternal outcome in terms of mortality & morbidity in cases of women in labour/postnatal women with sickle cell trait

• To study fetal outcome in terms of mortality & morbidity.

Objectives

- To compare the feto-maternal outcome of pregnant women in labour/postnatal women diagnosed with sickle cell trait, to that of feto-maternal outcome of CONTROL GROUP of pregnant women in labour/postnatal women with sickling negative, at the same institution.

• To detect the sickling status of the spouse to offer genetic counselling for future pregnancies

Material and Methods

Study Place: This retrospective study was carried out at Dhiraj General Hospital from 1stMay 2022 to 1stMay 2023.

Source of Data: A standard protocol is applied for all antenatal women, complete blood count and sickling test was carried out routinely. If sickling test was positive then haemoglobin electrophoresis

was carried out. All patients with positive sickle cell test were included under this study and the pregnancy outcome was compared with sickling negative patients.

Study Design: It was a retrospective, comparative, randomized study.

Sample size: 150 (75 control group, 75 case group)

Inclusion Criteria

1. Every pregnant woman registered at routine antenatal clinic of Dhiraj general hospital who is sickling positive and HB-electrophoresis suggestive of sickle cell trait irrespective of her gestation, parity & previous obstetrical outcome.

2. Every antenatal woman admitted to labour ward in emergency hours at Dhiraj General Hospital who is sickling positive and HB-electrophoresis suggestive of sickle cell trait irrespective of her gestation, parity & stage of labour.

3. Control subjects will be randomly sampled from a list of pregnant patients (approximately similar to study group with respect to age, parity, gestational age etc.) visiting the antenatal opd/came in labour at Dhiraj General Hospital between the same study periods but are not positive for SCT.

Exclusion Criteria

• Pregnancy with Sickle Cell Disease

• Pregnancy with SCT with other associated medical risk factors which can influence the course of pregnancy & its outcome like cardiovascular diseases, DM. etc

Result & Discussion

National & local SCT scenario

India tops the list of countries with sickle cell disease (SCD) with an estimated 44,000 live births in 2010 and a prevalence of 10%–33%[7].Gujarat comprises 10-15% of the tribal population of India, particularly Southern Gujarat and prevalence of sickle cell trait (SCT) varies from 0 to 31.4% among different tribal groups.[8] The tribal population is distributed in various districts of the state such as Sabarkantha, Banaskantha, Panchmahal, Vadodara, Narmada, Bharuch, Surat, Valsad, Dang and Div-Daman 8 SCT is frequently detected in tribal people such as Naika, Konkana, Rohit, Koli, Dubla ,Dhodia, Bhils, Gamit, [9] Our study was carried out in Dhiraj General Hospital, which is a rural tertiary health care facility, affiliated to SBKSMC&RC, located16 kms away from the Vadodaracity. My study was conducted at Dhiraj Hospitalsituated inWaghodiaTaluka ,Vadodara District which is a part of the TRIBAL BELT of Gujarat. Incidence of SCT and SCD As per this study, the incidence of SCT is 11.5% whereas that of SCD is 2.0%. These statistics include all the diagnosed ANC and PNC cases at this hospital irrespective of the booking status at the time of admission to labour ward.

Table 1: Booking status

Booked/Emg	Group			
	Case(HbS)		Control	
	Number	Percentage	Number	Percentage
Booked	53	70.0%	60	80.0%
Emergency	22	30.0%	15	20.0%
Total	75	100.0%	75	100.0%

Most of the patients were booked, in both the groups (70% in case group and 80% in control group).

Whereas emergency patients consisted of 30% vs 20%.

Table:2Parity

	Case		Control	
Parity	Number	N %	Number	N %
Primi	47	62.0%	49	66.0%
2	18	24.0%	15	20.0%
3	8	10.0%	6	8.0%
>4	2	4.0%	5	6.0%
Total	75	100.0%	75	100.0%
Chisquare:1.8858,pvalue:0.5964-NS				

Most of the patients were primigravida in both groups 62% vs 66%

Table:3 Haemoglobinlevel

	Case(HbS)		Control	
HB	Number	N %	Number	N %
< 6	7	8.0%	0	0.0%
6to10	32	45.0%	27	36.0%
>10	36	47.0%	48	64.0%
Total	75	100.0%	75	100.0%
Chisquare:6.835,pvalue:0.03279				

In patients with SCT, 45%. Of the patients had mild andmoderateanaemia.Thosewithsevereanaemia(8%)received Blood Transfusion. In control group, majority ofthepatientswerenot anaemic(64%.).

The incidence of anaemia is high in our study in SCTgroup.Probablecauseofthisishigherincidenceofcoexistingnutritionaldeficiencyanaemiaandlackofawareness about the disease in patients, as most of

thepatientsarefromlowsocioeconomicclassandtribalzone.Thesepatientshadpoorhygieneandmanyhad hookworminfestation.

Table:4AssociatedAntenatalComplications

AssociatedAntenatal Complications	Case		Control		
	Number	N%	Number	N%	P value
PregnancyInduced Hypertension	6	8.0%	1	2.0%	0.1 NS
IntrauterineGrowth Retardation	1	1.0%	1	2.0%	0.3 NS
Oligohydramnios	13	18.0%	5	10.0%	0.11 NS
Polyhydramnioswithcongenitalanomaly	2	3%	1	2.0%	0.12 NS
Anaemia	40	53.0%	18	36.0%	0.02 S
Recurrent UrinaryTractInfections	6	8.0%	0	4.0%	0.06 NS
Total	68	100%	26	56.0%	

The mostcommonassociatedAntenatalcomplicationsencountered is anemia.In case group it is53%, whereas incontrolgroup, it is36%.Inourstudy,amongtheassociatedAntenatalcomplications,inSCTgroupPIHwasfoundin8%patients,intrauterinegrowthretardationin1%,oligohydramnios in 18%, polyhydramnios with congenitalanomalyin 3.0%,anaemiain53%and recurrentUTIin8% of case group whereas in control group it was 2%,2%, 10%, 2%, 36%, 4% respectively.

Table:5Gestational Age (GA) at the time of labour

	Case		Control	
GA by LMP	Number	Percentage	Number	Percentage
<22 weeks	2	2%	0	0%
22-28 weeks	0	0%	0	0%
28-32 weeks	6	8%	1	2%
33-36 weeks	29	39%	8	16%
37-40 weeks	38	51%	66	82%
Chisquare:21.6433, pvalue:0.0023-S				

In case group, mostly the patients had preterm delivery47% whereas in control the patients was delivered at term 82%

Table:6Pregnancyoutcomes

	Case		Control		
Pregnancy Outcome	Number	Percentage	Number	Percentage	P value
IUGR	1	1.0%	2	4.0%	
Preterm	36	47.0%	10	20.0%	0.0008S
Postterm	1	2.0%	2	4.0%	
Abortion	1	1.0%	0	0.0%	
Stillbirth	1	1.0%	0	0.0%	
Intrauterine demise	0	0.0%	0	0.0%	
Term	35	48.0%	36	72.0%	0.002S

In this study, most of the deliveries were preterm, 47% inSCT group, whereas in control group,term deliveries72%,wasacommonoutcome. OurstudycorelateswithTaylorstudy.[10]Thepretermdelivieswassignificantlymore47%incase groupversus 20% in control group. This is a tertiary centre andmostlythepatientsarebooked,sothepercentageofIUD **i**s nil in both groups and still birth and abortion is alsorelatively less

Table:7 Intrapartum Interventions

	Case		Control		
Management in Labour	Number	Percentage	Number	Percentage	P value
BT given	6	8.0%	2	3%	
EPISOTOMY	50	50.0%	30	40.0%	
ICU Admission due to anaesthetic complication	2	2.0%	0	0%	0.31 NS
Augmentation with oxytocin	8	10.0%	3	4.0%	0.4 NS
OXYGENATION, HYDRATION	9	12.0%	0	0.0%	0.01 S
Chisquare:3.5182, pvalue:0.4751-S					

In labor SCT group and control group both were given episiotomy 50% vs 40% respectively as most of the patients were primigravida and most of it was preterm deliveries.

Table:8Modeof Delivery

	Case		Control		
Mode Of Delivery	Number	Percentage	Number	Percentage	P value
Caesarean section	23	30%	18	24%	0.49 NS
Spontaneous vaginal delivery	45	60%	52	68%	0.29 NS
Assisted Vaginal (Vacuum delivery)	2	3%	1	2%	
Assisted Vaginal (Forceps delivery)	5	7%	4	6%	
Total	75	100%	75	100%	
Chisquare:1.559, pvalue:0.6686-NS					

In case group, mode of delivery included most commonly vaginal delivery 60% vs 68% in control group.

Table:9 New born birth weight

	Case		Control	
Birth weight	Number	Percentage	Number	Percentage
<999 gms	1	2%	1	0%
1.0 to 1.5 kg	6	8%	3	4%
1.5 to 2.5 kg	31	41%	13	18%
≥2.5 kg	37	49%	58	78%
Total	75	100%	75	100%
Chisquare:13.0057 , pvalue:0.0046-NS				

Most of the new born were low birth weight 49% , whereas in control nearly 78% new born were

more than 2.5 kg.

Table10:PostpartumComplications

PostpartumComplains	Case		Control	
	Number	N%	Number	N%
PPH	6	8.0%	2	4.0%
LegCramps	9	12.0%	0	0.0%
WoundInfection	2	2.0%	1	2.0%
Perinealtear	3	4.0%	1	2.0%
Fever	12	16.0%	1	2.0%
ChiSquare:2.353,pvalue:0.6711–NS				

In case group, the most common postpartum complaint wasfever16%vs2%incaseandcontrolgrouprespectively.Incontrolgroupthemostcommonpost-partum complaint was post-partum haemorrhage, 8%. Ourstudy co relates with Abdulsalam study[11]and is stasticallysignificant in case of fever. In other complications it isnon-significant.

1. The most common post-partum complication includedfever in case group 16% and 2% in control group.Therewasduetodevelopmentofpostpartumendometritis in 3 patients. And puerperal pyrexia waspresent in 7 of our patients and 2 patient developedpuerperal sepsis. Intravenous antibiotic was given tothese patients which helped in faster recovery.Thiswas due to poor hygiene and poor nutritional status ofthepatient.
2. There was also a case of wound infection followingcaesareans section. This was due to poor hygiene ofthepatientandthepatienthadsevereanaemia.
3. PPHwaspresentin8%ofcasegroupand4%incontrolgroup.2 followingvaginaldeliveryand4followingcaesareansection.Thesepatientsweremanaged and recovered well.
4. Leg cramps was observed in 12% of SCT group withnoneincontrolgroup.Theyweregiven symptomatic treatment.USGoflegswerecarriedoutandDVTwasruledout.Noneof themsuffered fromDVT.
5. Perinealtearwasseenin4%ofcasevs2%incontrolgroup(table10)

ThereWasNoMaternalMortalityInSctGroupAndNonSctGroup.

Table11:Spousesickling

	Case(SCTpositive)	
SpouseSickling	Number	Percentage
NotKnown	31	42.0%
Negative	35	46.0%
POSITIVE	9	12.0%
Total	75	100.0%

It was found that 12% of the Spouse were sickling positiveinSCTgroup.Amongtheseallweresicklecelltrait.However, 42% patients' spouse didn't agree for the test.Controlincluded sicklingnegative.

Thiswascarriedoutonlyincasegroup.Thesicklingstatuswasnotknownin42%astheywereunwilling .Negative in 46% patients' spouse. Positive in 12%. Theseallweresicklecell trait.

In this study, spouse sickling was also done along withpatient in order to find out the chances of transmission tooffspring. Genetic counselling was offered and it was leftfor the patient and her family to decide upon the future ofpregnancy. Apart from all spouse sickling studied 12%were sickling positive. Among these all were sickle celltrait.Around 46% spouseofdiagnosedSCTandSCDpatients refused for this test. This was because most of ourpatients are tribal, low socio economic patients. They lackeducation and are non-affording. So, this test could not becarriedout inthem.

Conclusion

Sickle Cell Trait is considered a benign state. However,pregnancy is itself a stressful situation so these patientsrequiretertiaryhealthcaretodealwiththecomplications & disapproves the null hypothesis that was antenatal, intranatal,andpostnatalcourseofpregnancyinwomendiagnosedwithsicklecelltraitiscompara blewithpregnantwomen withoutsicklecelltrait.

TheSickleCellTraitpatientsshouldundergoANCregistrationasearlyaspossibleandshouldgof orinstitutional deliveries with NICU and blood bank facility.First of all, a regular, vigilantand meticulous antenatalcare,closeobservationcoupledwithmulti-disciplinaryapproach is necessary to get healthy mother and healthybaby in these patients.It should be aimed to avert, detect& abort all possible complications, during this period, toobtainthebestpossiblematernal&perinataloutcome.

Expertintrapartummanagementisneededtorescueimpeding morbidities and mortalities to

mother and foetus.SickleCellTraitcanbeanimportantcontributorforadversematernalandperinataloutcome.So,theAshaworkersshouldbetrainedtotacklepost-partumcomplicationsin thesepatients.

Acounsellingcentreshouldbeavailableatthehospitalwith special provision for the spouse ofSCT patients to undergo sickling test and Hb electrophoresistest to be made free of cost. The test if positive, geneticcounselling should be provided to the couple before orafterconception.

References

1 IanDonald'sPracticalObstetricProblems,seventhedtion,2017©RenuMisra,pg209-210)

2 Milner, P. F., B. R. Jones, and J. Döbler. "Outcome ofpregnancyinsicklecellanaemiaandsicklecell-haemoglobinCdisease.Ananalysisof181pregnanciesin98patients,andareviewofthelite rature."*Americanjournalofobstetricsandgynaecology*138.3 (1980):239-245.

3 Sears, David A. "The morbidity of sickle cell trait: areviewoftheliterature."*TheAmericanjournalofmedicine*64.6 (1978): 1021-1036.

4 Stockman,JamesA.,etal."Occlusionoflargecerebral vessels in sickle-cell anaemia." *New EnglandJournalofMedicine*287.17(1972):846-849.

5 Tsaras and co-workers,2009 Barahimi, Behin, Ann P.Murchison,andJurijR.Bilyk."Forgetmenot."*Surveyofophthalmology*andgynaecology55.5(2010):467-480.

6 Origin and Distribution of Sickle Cell Disease- HealthCareProviders-TheChildwithSickleCellDisease

7 lah,Roshan&Mukherjee,Malay&Ghosh,Kanjaksha.(2014).SicklecelldiseaseinIndia.Currentopinion inhematology

8 SaxenaD,YasobantS,GolechhaM.Situationalanalysis of sickle cell disease in Gujarat, India. IndianJCommunity Med2017;42:218-21

9 Kaur,Manpreet&Dangi,Cbs&Singh,M&Singh,H & Kapoor, S. (2013). Burden of sickle cell diseaseamongtribesof India

10 Pregnancy loss after first-trimester viability in womenwith sickle cell trait: Time for a reappraisal?Authorlinksopenoverlaypanel<u>MichelleY.TaylorMD[a]JosephineWyatt-AshmeadMD[b]JermaineGrayMD[a]JamesA.BofillMD[a]RickMartinMD[a]JohnC.MorrisonMD[a]</u> DepartmentsofObstetricsandGynecologyPathology,UniversityofMississippiMedicalCenter,Jackson,MSReceived1July2005,Revised4January2006,Accepted15 February2006,Availableonline25April2006

11 PregnancyoutcomesamongPalestinianrefugeeswomen with sickle cell trait in Damascus Asma A.Abdulsalam, PhD, Hyam N. Bashour, PhD, Fawza S.Monem, PhD, FathiM. Hamadeh, MSc,SaudiMed J2003;vol24(9)