ISSN: 2581 – 3633
PubMed - National Library of Medicine - ID: 101745081

International Journal of Medical Science and Advanced Clinical Research (IJMACR)

Available Online at: www.ijmacr.com

Volume – 3, Issue – 2, March - April - 2020, Page No. : 153 - 160

Influence of Sickle Cell Trait on Pregnancy Outcome

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Type of Publication: Original Research Article

Conflicts of Interest: Nil

Abstract

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 prospective study was carried out at Dhiraj General Hospital for one and a half year.

Source of Data: All patients who were sickling positive were included under this study and the pregnancy outcome was compared with sickling negative patients.It is a comparative, non- randomized study.

The percentage of SCT in ANC patients is 11.5% and SCD IS 2.0% whereas in total number of deliveries, SCT is 11.5% and SCD is 2.1% which is comparatively high.

Socio demographic data remains same in both groups. The most common pregnancy outcome in SCT is preterm deliveries 46%, new borns were mostly preterm 52% and required NICU admission 66%. Maternal morbidity was 36% among SCT group and there was no maternal mortality.

Sickle Cell Trait is considered a benign state. However, pregnancy is itself a stressful situation so these patients require tertiary health care to deal with the complications & disapproves the null hypothesis that was antenatal, intranatal, and postnatal course of pregnancy in women diagnosed with sickle cell trait is comparable with pregnant women without sickle cell trait.

Last but not the least, regular and meticulous antenatal care, close observation coupled with multi-disciplinary approach is necessary to get healthy mother and healthy baby in these patients

Keywords: Sickle Cell Trait, Hemoglobin S, Haemoglobin A, Heterozygous, Preterm Deliveries, Enign State, Multi-Disciplinary Approach

Introduction

The core of the antenatal care programs was developed in the early 20th century. 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.1Test for detection of Sickle cell being one of them, as 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

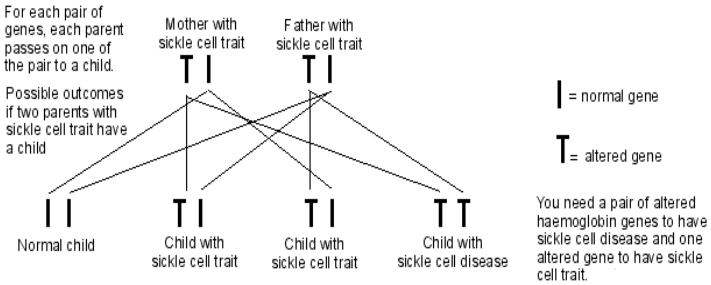
Sickle cell anaemia include both sickle cell disease and sickle cell trait. The first one is homozygous form with SS genotype whereas the latter on is heterozygous form Ss. In this both MCV and MCHC is reduced. Due to the presence of Hb S these patients are subjected to chronic hypoxia. Sickle cell trait 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 2nd/3rdtrimester 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.[6]

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, and hyposthenuria[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 fetal outcome in terms of mortality & morbidity.
- To study maternal outcome in terms of mortality & morbidity in cases of women in labour/postnatal women with sickle cell trait.

Objectives

- To detect the sickling status of the spouse to offer genetic counselling for future pregnancies.
- 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 normal pregnant women in labour/postnatal women, at the same institution.

Material and Methods

Study Place: This prospective study was carried out at Dhiraj General Hospital from February 1st 2018 to July 2019.

Source of Data: A standard protocol is applied for all antenatal clients, 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 prospective, comparative, non-randomized study.

Sample size: 100 (50 control group, 50 case group)

Inclusion Criteria

1. Every pregnant woman registered at routine antenatal clinic of Dhiraj general hospital that shows SCT on Electrophoresis irrespective of her gestation, parity & previous obstetrical outcome.
2. Every registered or unregistered pregnant woman admitted to labour ward in emergency hours at Dhiraj General Hospital that shows SCT on Electrophoresis 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 clinic/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]. About 10-15% of the tribal population of India is in Gujarat, particularly in South Gujarat and prevalence of sickle cell trait (SCT) varies from 0 to 31.4% among different tribes.[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 Bhils, Gamit, Dhodia, Dubla, Koli, Naika, Rohit, Konkana[9]

Our study was carried out in Dhiraj General Hospital, which is a rural tertiary health care facility, affiliated to SBKSMC&RC, located,16 kms away from the Baroda city. It covers an area of around 7,550 sq kms of rural areas. The location of the S.B.K.S.Medical & Research institute is in the Waghodia Taluka of Baroda 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 figures include all the diagnosed ANC and PNC cases at this institute 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	33	66.0%	40	80.0%
Emergency	17	34.0%	10	20.0%
Total	50	100.0%	50	100.0%

Most of the patients were booked, in both the groups (66% in case group and 80% in control group)

Table: 2 Haemoglobin level+

	Case(HbS)		Control	
HB	Number	N %	Number	N %
< 6	6	12.0%	0	0.0%
6 to 10	21	42.0%	18	36.0%
> 10	23	46.0%	32	64.0%
Total	50	100.0%	50	100.0%
Chi square: 7.07, p value: 0.02-S				

In patients with SCT, 54%. Of the patients had mild and moderate anaemia. Those with severe anaemia (12%) received Blood Transfusion. In control group, majority of the patients were not anaemic (64%.).

The incidence of anaemia is high in our study in SCT group. Probable cause of this is higher incidence of coexisting nutritional deficiency anaemia and lack of awareness about the disease in patients, as most of the patients are from low socio economic class and tribal zone. These patients had poor hygiene and many had hookworm infestation.

Table: 3 Urine Routine/ Microscopy

	Case(HbS)		Control	
Urine Routine/Microscopy	Number	N %	Number	N %
ALB TRACE	1	2.0%	1	2.0%
ALB +1	3	6.0%	0	0.0%

ALB +2	1	2.0%	0	0.0%
>ALB+3	4	8.0%	0	0.0%
PUS CELLS++	4	8.0%	1	2.0%
NORMAL	37	74.0%	48	96.0%
Chi square: 10.4, p value: 0.06-NS				

Mostly the patients in case group and control group were asymptomatic, 80% vs 96% respectively. In SCT, 8% patients presented with UTI.

In case group, though Recurrent UTI was not common, it was found in 12% patients. Asymptomatic bacteriuria was present in these cases. Whereas in control group it was only 4%. High albumin levels was also present in pre-eclampsia patients. (p value 0.06)

Table: 4 Associated Antenatal Complications

Associated Antenatal Complications	Case		Control		
	Number	N %	Number	N %	P value
Pregnancy Induced Hypertension	4	8.0%	1	2.0%	0.1 NS
Intrauterine Growth Retardation	1	2.0%	1	2.0%	0.3 NS
Oligohydramnios	10	20.0%	5	10.0%	0.11 NS
Polyhydramnios with congenital anomaly	2	4.0%	1	2.0%	0.12 NS
Anaemia	27	54.0%	18	36.0%	0.02 S
Recurrent Urinary Tract Infections	6	26.0%	0	0.0%	0.06 NS
Total	50	100%	26	52.0%	
Chi square: 4.46, p value: 0.48-NS					

The most common associated Antenatal complications encountered is anemia.In case group it is 54%, whereas in control group, it is 36 % .

In our study, among the associated Antenatal complications, in SCT group PIH was found in 8% patients, intrauterine growth retardation in 2%, oligohydramnios in 20%, polyhydramnios with congenital anomaly in 4%, anaemia in 54% and recurrent UTI in 12% of case group whereas in control group it was 2%, 2%, 10%, 2%, 36%, 4% respectively. The p value is non-significant

Table: 5 Pregnancy outcomes

	Case		Control		
Pregnancy Outcome	Number	Percentage	Number	Percentage	P value
IUGR	1	2.0%	2	4.0%	
Preterm	26	52.0%	10	20.0%	0.0008 S
Post term	1	2.0%	2	4.0%	
Abortion	1	2.0%	0	0.0%	
Still birth	1	2.0%	0	0.0%	
Intrauterine demise	0	0.0%	0	0.0%	
Term	21	42.0%	36	72.0%	0.002 S
Chi square: 13.7, p value: 0.017-S					

In this study, most of the deliveries were preterm, 52% in SCT group, whereas in control group, term deliveries, 72%, was a common outcome.

Our study co relates with Taylor study.[10] The preterm deliveries was significantly more 52% in case group versus 20% in control group. This is a tertiary centre and mostly the patients are booked, so the percentage of IUD is nil in both groups and still birth and abortion is also relatively less

Table 6: Analysis of NICU Admission

Causes	Case Number		Control	
Preterm care	11	28.0%	2	4.0%
Birth Asphyxia	6	12.0%	5	10.0%
Transient Tachypnoea of	2	4.0%	3	6.0%

New born				
IUGR	1	2.0%	0	0.0%
Sepsis	2	4.0%	1	2.0%
Congenital Anomaly	2	4.0%	0	0.0%
PT with RDS	3	6.0%	0	0.0%
Neonatal hyperbilirubinemia	1	2.0%	4	8.0%
Chi Square: 11.8 , p value: 0.1072 –NS				

The most common cause of NICU admission in case group is preterm 28%. In control group it is for birth asphyxia 10%

NICU admission, causes of admission & neonatal death

1. As per this study, the percentage of new born requiring NICU admission was 66% in case group whereas in control group it was 30%.
2. The most common cause of NICU admission in case group was for preterm care 28% vs 4% in control group. Remaining causes included birth asphyxia 12% vs 10%, TTN 4% vs 6%, IUGR 2% vs 0%, sepsis 4% vs 2%, congenital anomaly 4% vs 2%, Preterm care with RDS 6% vs 0%, neonatal hyperbilirubinemia 2% vs 8%. Most commonly preterm deliveries was seen in case group requiring NICU admission for preterm care.

Other causes included birth asphyxia, TTN (transient Tachypnoea of new born), IUGR, and for congenital anomalies which was associated with polyhydramnios. . Neonatal hyperbilirubinemia was more common in control group as they were term deliveries .

3. Among these 12% was neonatal death in case group and 4% in control group (table 6) This is statically significant. The cause of neonatal death in case group included, 2 deaths due to respiratory distress syndrome in preterm premature babies. 2 deaths due to severe birth asphyxia 1 death due to congenital anomaly (spina bifida) 1 death due to early onset of sepsis. In control group, 2 deaths occurred due to severe birth asphyxia.

Table 7: Postpartum Complications

Postpartum Complains	Case		Control	
	Number	N %	Number	N %
PPH	4	8.0%	2	4.0%
Leg Cramps	5	10.0%	0	0.0%
Wound Infection	1	2.0%	1	2.0%
Perineal tear	2	4.0%	1	2.0%
Fever	7	14.0%	1	2.0%
Chi Square: 2.667 , p value: 0.44 –NS				

In case group, the most common postpartum complaint was fever 14% vs 2% in case and control group respectively. In control group the most common post-partum complaint was post-partum haemorrhage, 4%. Our study co relates with Abdulsalam study[11] and is stastically significant in case of fever. In other complications it is non-significant.

1. The most common post-partum complication included fever in case group 14% and 2% in control group. There was due to development of postpartum endometritis in 2 patients. And puerperal pyrexia was present in 4 of our patients and 1 patient developed puerperal sepsis. Intravenous antibiotic was given to these patients which helped in faster recovery. This was due to poor hygiene and poor nutritional status of the patient.
2. There was also a case of wound infection following caesareans section. This was due to poor hygiene of the patient and the patient had severe anaemia.
3. PPH was present in 8% of case group and 4% in control group.2 following vaginal delivery and 2 following caesarean section. These patients were managed and recovered well.
4. Leg cramps was observed in 10% of SCT group with none in control group. They were given symptomatic

treatment. USG of legs were carried out and DVT was ruled out. None of them suffered from DVT.

5. Perineal tear was seen in 4% of case vs 2% in control group(table 7)

There Was No Maternal Mortality In Sct Group And Non Sct Group.

Table 8: Spouse sickling

	Case (SCT positive)	
Spouse Sickling	Number	Percentage
Not Known	22	40.0%
Negative	23	46.0%
POSITIVE	5	10.0%
Total	50	100.0%

It was found that 10% of the Spouse were sickling positive in SCT group. Among these all were sickle cell trait. However, 40% patients' spouse didn't agree for the test. Control included sickling negative.

This was carried out only in case group. The sickling status was not known in 40% as they were unwilling. Negative in 46% patients' spouse. Positive in 10%. These all were sickle cell trait.

In this study, spouse sickling was also done along with patient in order to find out the chances of transmission to offspring. Genetic counselling was offered and it was left for the patient and her family to decide upon the future of pregnancy. Apart from all spouse sickling studied 10% were sickling positive. Among these all were sickle cell trait. Around 40% spouse of diagnosed SCT and SCD patients refused for this test. This was because most of our patients are tribal, low socio economic patients. They lack education and are non-affording. So, this test could not be carried out in them

Conclusion

Sickle Cell Trait is considered a benign state. However, pregnancy is itself a stressful situation so these patients require tertiary health care to deal with the complications & disapproves the null hypothesis that was antenatal, intra natal, and postnatal course of pregnancy in women diagnosed with sickle cell trait is comparable with pregnant women without sickle cell trait.

The Sickle Cell Trait patients should undergo ANC registration as early as possible and should go for institutional deliveries with NICU and blood bank facility.

First of all, a regular, vigilant and meticulous antenatal care, close observation coupled with multi-disciplinary approach is necessary to get healthy mother and healthy baby in these patients.It should be aimed to avert, , detect & abort all possible complications, during this period, to obtain the best possible maternal & perinatal outcome.

Expert intrapartum management is needed to rescue impeding morbidities and mortalities to mother and foetus.

Sickle Cell Trait can be an important contributor for adverse maternal and perinatal outcome. So, the Asha workers should be trained to tackle post-partum complications in these patients.

A good counselling centre should be available in the institution and provision should be made for the spouse of SCT patients to undergo sickling and Hb electrophoresis test to be made free of cost. The test if positive, genetic counselling should be provided to the couple before or after conception.

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How to citation this article: Dr Piyusha Chandrayan, Dr Krishna Patel, Dr Usha Parekh, “Influence of Sickle Cell Trait on Pregnancy Outcome”, IJMACR- March - April - 2020, Vol – 3, Issue -2, P. No. 153 – 160.