WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.074
Volume 7, Issue 13, 1-15. Research Article ISSN 2277– 7105

STUDY OF SICKLE CELL DISEASE AND ITS RELATION TO MALARIA BETWEEN MARGINAL PEOPLE IN TAIZ(YEMEN)

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Article Received on
01 May 2018,

Revised on 22 May 2018,
Accepted on 12 June 2018,

DOI: 10.20959/wjpr201813-12708

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ABSTRACT

Aim: This study was carried out to determine the prevalence of sickle cell anemia and malaria at marginalized people(Al –akhdam-The neglected group) in different Areas in Taiz city, and relationship between sickle cell and age, sex& infection by malaria. **Study design**: Cross-sectional study. **Place and duration of study**: The study was carried out from areas in Taiz city for about 100 cases during February to April 2014, study population was the marginal people. **Methodology:** A total of 100 cases were randomly collected and examined by C.B.C, Sickling test, B.F.S. Also, the questionnaire data was used for determine the correlation between sickle cell and other factors such as age, sex, location, infected by malaria, blood transfusion prior and consanguinity. **Statistical analysis**: The data analyzed by SPSS program, and P value <0.05 was taken as significant. **Result:** The study found that 41 cases of sickle cell are positive for sickling test from total 100 specimens were collected from areas in Taiz city. Also found from 41 +ve sickling test, one case infected by malaria,17cases for male(39.5%)and 24 cases for female(42.1%) also32 cases (57.1%)with consanguinity and 22 cases (44%)with blood transfusion prior. The results of the study indicate that there is no significant different between age, location and the +ve sickling test, also indicate that there is significant relation between S.C. A. and kinship, infected by malaria previously and B.F.S. In this study there is no relation between malaria infection and S.C. anemia.

KEYWORDS: (Marginalized people; Taiz city- Yemen, Sickle cell disease, Malaria.).

Abbreviation

S.C.A: sickle cell anemia, B.F.S: blood film study,

C.B.C: Complete blood count I.S.C: irreversible sickle cell

S.C.D: sickle cell disease, MPS: Malaria parasite test.

EDTA: Ethylene diamintera- acetic acid

INTRODUCTION

In endemic countries, infection with *P. falciparum* causes a range of outcomes, including asymptomatic parasitemia, uncomplicated disease and severe malaria, which commonly progresses to death.[16]

After enduring 3years of war, hunger and disease, Yemenis could now be at heightened risk of catching malaria due to collapsing health care system.[23]

WHO estimated that malaria cases rose to 433000 from 336000 in 2016.

HbAS provides significant protection against both severe and uncomplicated malaria.[2] Case–control and cohort studies in multiple African countries have consistently found that HbAS is 75% protective against hospitalization for malaria.[20] Such asymptomatic malarial infections are important impediment to malaria control, because asymptomatic patients are not likely to seek treatment. Instead, these individuals continue transmitting the disease to others and provide a long-lasting reservoir for the malaria vector.[8,21]

With the increased movement observed in human populations, the high prevalence of asymptomatic infection increases the risk of malaria, particularly in malaria-free zones[2]. Individuals who carry the S-gene (sickle cell trait) have a reduced risk of experiencing symptomatic malaria infections, although sickle cell traits do not seem to the course of asymptomatic infections.[18,19]

The sickle cell trait is carried by individuals who inherit a normal hemoglobin gene from one parent (HbA) and a sickle hemoglobin gene (HbS) from the other, Sickle-cell disease occurs when an individual inherits the autosomal recessive S-gene (HbS) from each parent[13]. Sickle cell disease can cause multi-organ ischemic damage and deform red blood cells, which leads to anemia.[9]

People with sickle cell disease who live in rural Africa rarely survive to reproductive age.[5]

Malaria exerts substantial selective pressure on the human genome due to its high mortality and morbidity rates.[11] This selective pressure is believed to be responsible for the high prevalence of sickle cell disease in malaria-endemic regions.

In fact, approximately one third of all aboriginal inhabitants of Sub-Saharan Africa carry the S-gene.[6] As a result, 200; 000 infants are born with sickle cell disease in Africa each year, and in some areas of Sub-Saharan Africa, up to 2% of all children are born with sickle cell disease.[3]

SICKLE CELL and Malaria distribution in Yemen

YEMEN is located on the south west of the Arabian peninsula and has a population of 21 million. WHO estimated that malaria cases rose from 443000 to 336000 in 2016, it is estimated that the annual number of cases of malaria infection in Yemen are around 3million.

The overall prevalence of sickle cell trait[HbAS] in Yemen is 2.2% with a higher frequency in the mid-western region where Taiz city is located than in the central and eastern areas.

The prevalence of thalassemia trait in Yemen is13.3%[Beta thalassemia trait 4.4%, alpha thalassemia trait 8.9%, there are no previous reports on the occurrence of G6PD deficiency or thalassemia in Yemeni SCD patients, except one showing that the coexistence of alpha thalassemia in 26 Yemeni children with SCD living in Riyadh was 57.7%.[1]

MATERIALS AND METHODS

Study design, area and population

This is descriptive cross sectional case study aimed to determine CBC, blood films study, malaria and Sickling test in marginalized people.

Study population: 100 marginalized people at different ages.

Study area: Samples were collected from beerbasha, Alberara, Almadeenah alsakaneeyah + and other areas in Taiz city, Yemen.

Inclusion criteria: Marginalized people suspect suffering from anemia.

Ethics: The study was approved by the Research Ethics Committee of Faculity of Medicine and Health Sciences, Taiz University Yemen. Participation of patients was voluntary and obtaining informed consent from them before data and sample collection.

Time of study: Between February and April 2014 blood samples were collected from 100 marginalized people in Taiz city.

Specimen collection and processing[12]

5mL of venous blood were collected into EDTA tube and used for determination of complete blood count (CBC) using the sysmex, sickling test using the sodium meta bisulfate, Blood films were Stained with Giemsa stain. Malaria was indicated by presence of stages (Ring form, gametocytes) in thin and thick blood films.

Statistical analysis: Data was presented in form of tables and graphs by using spss.

Fig.1: Map of Yemen, show the areas risk with malaria.

RESULT

Table 1: Relation of Sickling test to age of examined cases.

		<10ys(%)	(11-13)ys%	(14-16) ys%	>17ys(%)	Total %
Sickling test	+ve	13 (43.3%)	12 (66.7%)	3 (37.5%)	13 (59.5%)	41 (41%)
	-ve	17 (56.7%)	6 (33.3%)	5 (62.5%)	31 (70.5%)	59 (59%)
	Total	30 (100%)	18 (100%)	8 (100%)	44 (100%)	100 (100%)

The No. of patients less than 10 ys shows +ve

Sickling test 13 cases (43.3%) from 30 cases but from (11-13ys) the sickling test were12cases (66.7%), also we notice from table 1 that the age from 14-16ys show less percentage of sickling test 8 cases (37.5%).

The total +ve sickling test was 41% from 100 examined cases. No significant relation(P

value more than 0.05).

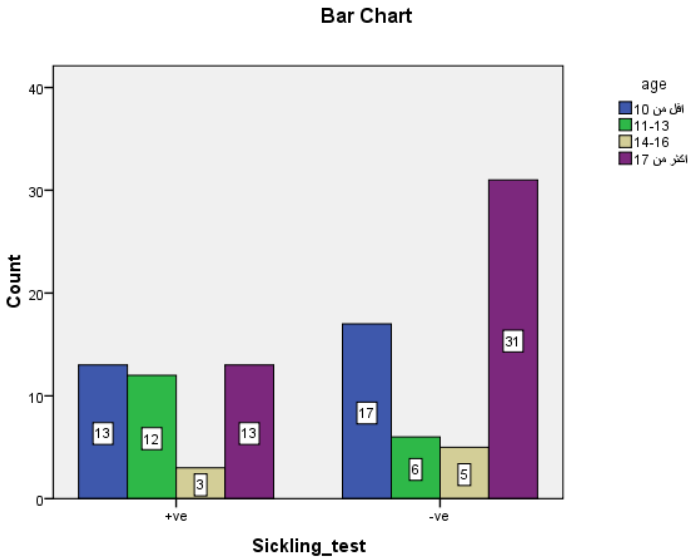

Figure 2: Relation of Sickling test to age of examined cases.

Table 2: Relation of Sickling test to sex of examined cases.

		Sex		Total %
		M %	F %	
Sickling test	+ve	17 (39.5%)	24 (42.1%)	41 (41%)
	-ve	26 (60.5%)	33 (57.9%)	59 (59%)
	Total	43 (100%)	57 (100%)	100 (100%)

From table 2: There was No significant relation between sex and positive sickling test (P value more than 0.05).

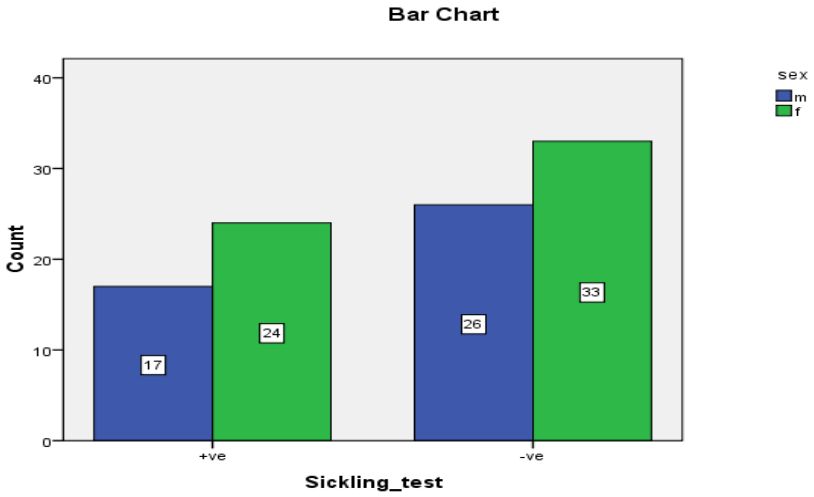

Figure 3: Relation of Sickling test to sex of examined cases.

Table 3: Relation of Sickling test to location of examined cases.

		Location					
		Beer_Basha %	**Alberara %**	**AlmadeenahAlsakaneyah %**	**Aldrbah %**	**Alshmacy %**	**Klabh %**
Sickling test	+ve	6 (46.1%)	1 (100%)	6 (42.9%)	10 (41.7%)	10 (38.5%)	5 (38.5%)
	-ve	7 (53.8%)	0 (0%)	8 (57.1%)	14 (58.3%)	16 (61.5%)	8 (61.5%)
Total		13 (100%)	1 (100%)	14 (100%)	24 (100%)	26 (100%)	13(100%)

		Location	
		Alsaha %	**Total %**
Sickling test	+ve	3 (33.3%)	41 (41%)
	-ve	6 (66.6%)	59 (59%)
	Total	9 (100%)	100 (100%)

From the table 3, There was No significant difference, between regions and sickling test(P value more than 0.05).

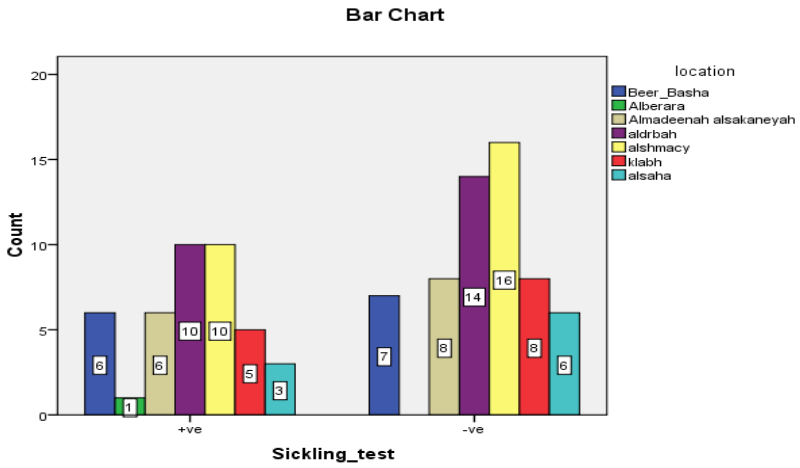

Figure 4: Relation of Sickling test to location of examined cases.

Table 4: Relation of Sickling test to kinship(consanguinity).

		Kinship		
		yes	**No**	**Total %**
Sickling test	+ve	32 (57.1%)	9 (20.5%)	41 (41%)
	-ve	24 (42.9%)	35 (79.5%)	59 (59%)
	Total	56 (100%)	44 (100%)	100 (100%)

Table 4: There was strong significant different between the sickle cell diseases and the kinship(consanguinity) (P value less than 0.0 5).

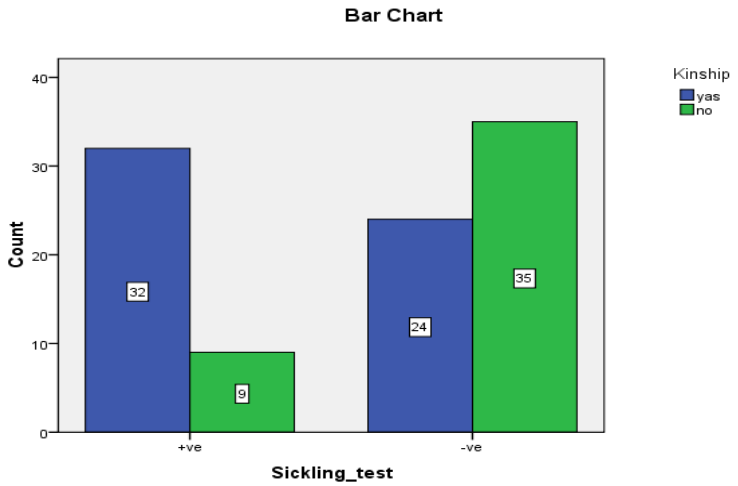

Figure 5: Relation of Sickling test to kinship(consanguinity).

Table 5: Sickling test in relation to Blood transfusions prior.

		Yes	No	Total
Sickling test	+ve	22 (44%)	19 (38%)	41 (41%)
	-ve	28 (56%)	31 (62%)	59 (59%)
	Total	50 (100%)	50 (100%)	100 (100%)

Table 5: No Significant relation between +ve sickling test and Blood transfusion prior(p>0.05).

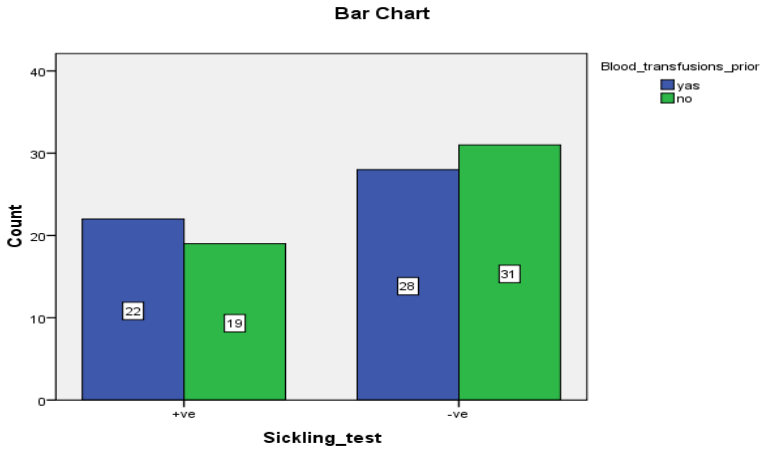

Figure 6: Sickling test in relation to Blood transfusions prior.

Table 6: Relation of Sickling test to infection with malaria previously.

		Infected by malaria in past		
		Yes %	no	Total
Sickling test	+ve	8 (22.2%)	33 (51.6%)	41 (41%)
	-ve	28 (77.8%)	31 (48.4%)	59 (59%)
	Total	36 (100%)	64 (100%)	100 (100%)

From the table 6 the percentage of the infected cases by malaria previously in relation to +ve sickling test were 8 cases(22.2%) Whereas the percentage of +ve sickling test in cases not infect with malaria previously was 33cases(51.6%). There was significant different(P value less than 0.0 5).

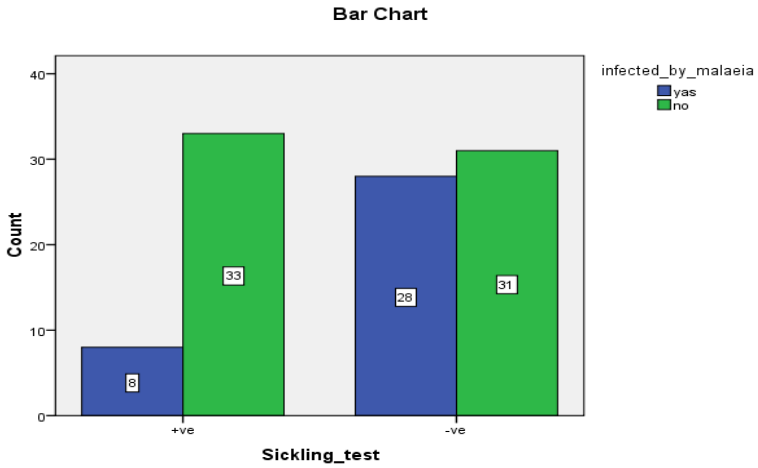

Figure 7: Relation of Sickling test to infection with malaria previously.

Table 7: Relation of Sickling test to HB of examined cases.

			HB				
		<12		12-17		Total	
Sickling test	+ve	18	66.6%	23	31.5%	41	41%
	-ve	9	33.3%	50	68.4%	59	59%
	Total	27	100%	73	100%	100	100%

From table 7, We noticed that the percentage of +ve sickling test cases which had HB less than 12mg/dl was18 cases(66.6%), but 23case(31.5%) +ve sickling cases had HB more than 12mg/dl, P value less than 0.05(sig. different).

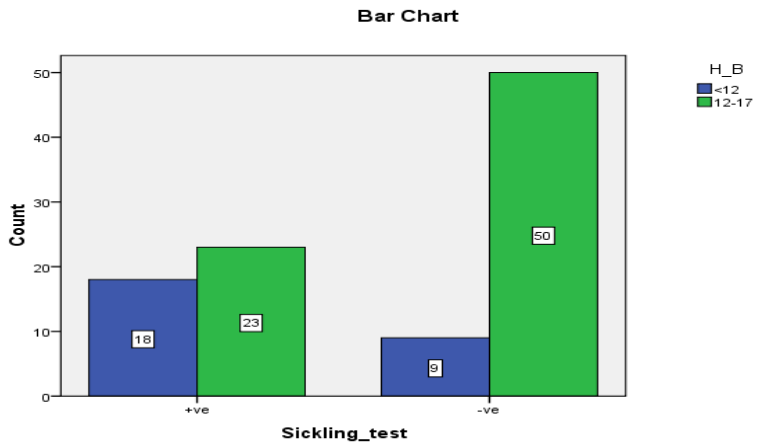

Figure 8: Relation of Sickling test to HB of examined cases.

Table 8: Sickling test in relation to BFS.

		BFS				
		Normocytic normochromic	**Michrocytic hypochromic**	**Sickle cell**	**poikilocytosis**	**Total**
Sickling_test	+ve	24(57.1%)	0(0%)	12(29.2%)	5(12.1%)	41(41%)
	-ve	55(93.3%)	4(6.7%)	0(0%)	0(0%)	59(59%)
	Total	79(93.3%)	4(6.7%)	12(29.2%)	5(12.1%)	100(100%)

From the table 8, the percentage of +ve sickling cases which had normochromic normocytic blood film was 24cases(57.1%) and 5case(12.1%) +ve sickling cases showed poikilocytosis, and the reminder +ve sickling cases showed sickling cells (29.2%),there was significant different between the sickle cell disease and the change in the blood film for the size, amount of cell and HB(P value less than 0.05).

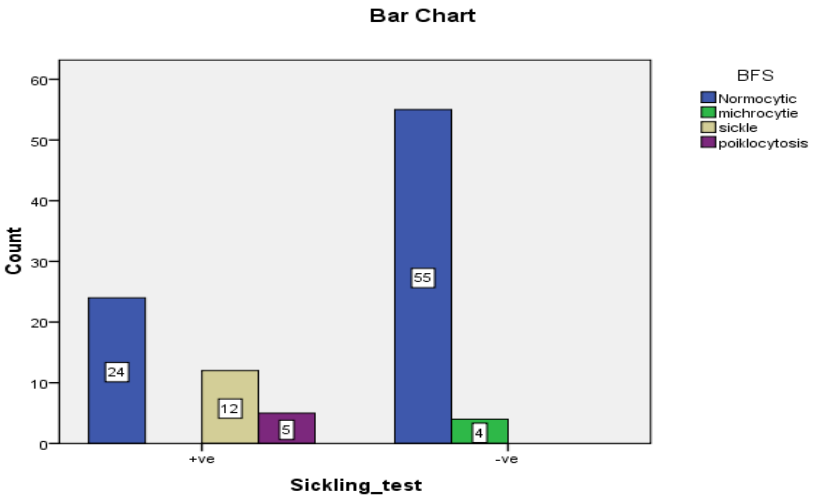

Figure 9: Sickling test in relation to BFS.

Table 9: Sickling test in relation to MPS.

		MPS					
		+ve	**(%)**	**-ve**	**(%)**	**Total**	**(%)**
Sickling test	+ve	1	(33.3%)	40	(41.2%)	41	(41%)
	-ve	2	(66.6%)	57	(58.8%)	59	(59%)
	Total	3	(100%)	97	(100%)	100	(100%)

Table 9: the percentage of the +ve malaria in blood film study in relation to +ve sickling test was 33,3% whereas the –ve malaria in B.F.S. in relation to +ve sickling test was 41.2%. There was no significant different (P value more than 0.05).

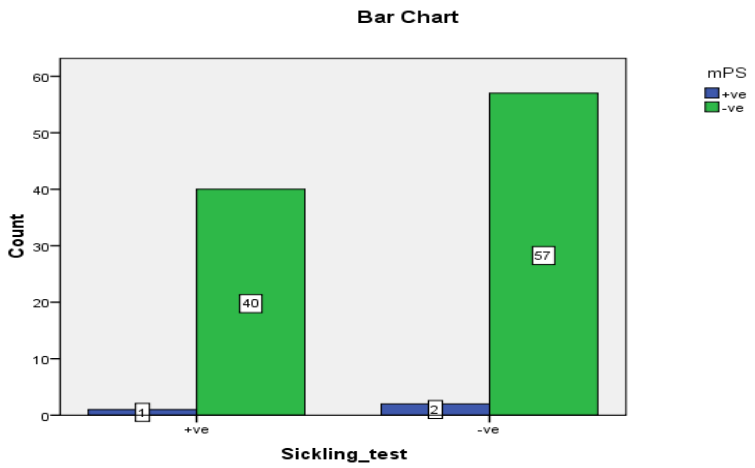

Figure 10): Sickling test in relation to MPS.

DISCUSSION

As Thomas et al[17], said that anemia is a common sequel of malaria infection but is often clinically silent, as such, it likely makes a large but hidden contribution to overall mortality due to malaria, especially in young children.

Malaria is believed to be a major cause of morbidity in SCD patients, it is a precipitating factor for the frequent vaso occlusive crises experienced by these patients; and may thus be responsible for hospital admission, it is customary, therefore, to prescribe malaria chemoprophylaxis for almost every SCD patient who is in crisis regardless of whether they are symptomatic or not(Rachel Kotila et al.[14]

In our result, table 1 shows the relation of sickling test to age of examined cases. The No of patients less than 10 years shows positive sickling test 13 cases (43.3%) from 30 cases but from (11-13 years) the sickling test was 12 cases (66.7%), also we notice from table 1 that the age from 14-16 years shows less percentage of sickling test 8 cases (37.5). The total positive sickling test was 41% from 100 examined cases. No significant relation between sickling test and age in our study (p value more than 0.05).

Studies in Kenya by Charlotte et al[7], disagree with our study they showed that the prevalence of SCA decreased from 8 of 782cases (1.0%) in children younger than 12 months to 2 of 697 cases(0.3%) in children 12 to 59 months of age, in their studied there was significant relation between sickle cell and age $p < 001$.

G Ndeezi et al[26] found in their study that S.C.D contributes to mortality in children younger than 5years in sub-Sahran area(Uganda).

Table 2 of our result shows the percentage of males with positive sickling test was 39.5% whereas the percentage in females with positive sickling test was 42.1%, there was no significant relation between test and sex. (p value more than 0.05), Direwprovein Andrew[13], said that no relation between the sickle cell disease and sex. Also E Elguero et al[25], in their study in Gabon agree with our result, that no relation between S.C trait and sex.

Table 3 of our result shows the percentage of positive sickling test was 46.1% in Beer basha, in Alberara 1%, in Almadenah Al sakaneeyah 42.9%, in Aldrbah 41.7%, in Al Shmacy 38.5%, in Kalbh 38.5% and in Al Saha 33.3% respectively, where malaria is endemic there. We found no significant relation between sickle cell anemia and locations (P value more than 0.05).

But in the other study done by Sutaoevined[15], in Maharashtra (Gazette of Maharashtra) only six districts are endemic to malaria. These districts prone to malaria in Maharashtra are Thane, Raigad, Nasik, Gondia, Chandrapur, Gadchiroli and Gr. Mumbai.

There, patients with sickle cell anemia are prone to various types of infections included malaria, which are endemic in this environment, and according to Al Juwah et al[4] studied, they found that no relation between districts, malaria and sickle cell disease.

We found in our result strong significant different between the sickle cell diseases and the kinship(consanguinity) as shown in the table 4.

These show that the percentage of the kinship between the positive sickling cases was 32 cases (57.1), whereas the percentage of positive sickling cases without kinship was 9 cases (20.5%) (P value less than 0.05),the study of Aw Al-Saqladi[24], in Yemen showed that, relation of consanguinity and the inherited diseases like sickle cell is strong.

Sickle cell disease is an inherited disorder that has its cardinal features chronic hemolytic anemia and recurrent painful episodes as explained in Hematology Basis by Roland.[10]

Our study shows that, there was no relation between sickle cell diseases and blood transfusion prior, P value was more than 0.005 as shown in table 5, same like that mentioned

by Direwprovein Andrew.[13] But in same reference mentioned the relation between malaria and blood transfusion prior is positive.

From the table 6 in our result shows the percentage of the infected cases by malaria previously in relation to positive sickling test was 8 cases (22.2%) whereas the percentage of the positive sickling test but not infect with malaria previously was 33 cases (51.6%). There was significant different (p value less than 0.05).

A number of mechanisms explained the previous result of us, First, parasite –infected HbAS erythrocytes have been shown to sickle 6 times more readily than non-parasitized HbAS cells, a phenomenon that may lead to intracellular parasite death and/or their enhanced removal by the immune system, recent data have suggested that acquired immunity may also be involved as mentioned by Thomas et al.[17]

Table7 in our study shows that the percentage of positive sickling test cases which had HB less than 12 mg/dl was 18 cases (66.6%),but 23 cases (31.5%) of positive sickling cases had HB more than 12mg/dl, p value less than 0.05 (significant different), Anisa and Kwabena[22], found in their study in Yemen that HbAA children is higher Hb than HbAS children affected by malaria, also in their study, they found that HbAS showed more significant hematological alteration than HbAA.

In Nigerian children however, sudden and severe anemia accompanied by features of imminent heart failure suggested aplastic or sequestration crises as mentioned by Al Juwah et al.[4]

Two factors correlate best with the development of severe anemia: hemoglobin level preceding the malaria transmission season and the parasite density achieved during incident infection, it seems likely that children with HbAS enjoy a double advantage in this regard: first, because they suffer fewer clinical attacks of malaria, their baseline hemoglobin levels may be higher; and second, they may be further protected by the lower parasite densities achieved during incident infection as described by Thomas et al.[17]

Table 8 of our result shows the percentage of positive sickling cases which had normochromic normocytic blood film was 24 cases (57.1%) and 5 cases (12.1%) positive sickling cases showed poilkilocytosis, and the reminder positive sickling case showed sickling cells 12 cases (29.2%), there was significant different between the sickle cell disease

and the change in the blood film for the size, amount of cell and HB (p value less than 0.05), Anisa and Kwabena[22] said that HbAS showed significant hematological alteration than HbAA, and this agree with our result.

Also in Monica[12] mentioned that the thin blood film shows marked Poikilocytosis with sickle cell, nucleated red cells, and target cells, macrocytes may also be present due to folate deficiency, there is a marked polychromasia due to a high reticulocyte count.

Table(9) in our result shows, the percentage of the +ve malaria in blood film study in relation to +ve sickling test was 33,3% whereas the –ve malaria in blood film study in relation to +ve sickling test was 41.2%. there was no significant different (P value more than 0.05). E Elguero et al[25], did study on 3,959 patients from 195 villages in Gabon agree with our study, they found that malaria disease had no relation with SC trait, they said an increase of 10% 0f *P.falciparum* in patients is associated with increased by 4.4% of SC trait. Also study done by Thomas et al[17] agree with our result, they found that HbAS had no effect on the prevalence of symptomless parasitemia but was 50% protect against mild clinical malaria.

Recommendation Conclusion and

1- From the study above, we found that HbAS had no relation with parasitemia but make protection against malaria, we advise to continue the researches about types of S.C.A. in marginal people and its relation to malaria.
2- Also we found that still the sickle cell disease and malaria consider as a big health problem in Yemen, malaria is great spread specially in this war time.
3- We advise to do examination for the pre-marriage to limit the establishment of sickle cell anemia.

KNOWLEDGEMENT: Thanks for Dr. Radfan, Watheq, Mushera and Azza.

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