DISCUSSION
The population of India exhibits a wide range of genetic heterogeneity, ecological and biological diversity. Hemoglobinopathies are the most commonly encountered monogenic disorders of blood posing a major genetic and public health problem in Southeast Asia and the Indian subcontinent. The finding of different hemoglobinopathies prevalent in the state is in agreement with its population admixture. There were three waves of migration that entered through Northern, Eastern and Western corridors of the state. The northern waves (i.e. Bramhins of Orissa have been said to be migrated from the state of Uttar Pradesh) have brought the β-thalassemia gene, the Eastern migrants from West Bengal and Assam came with Hemoglobin E, and the Western people with sickle cell gene in Orissa from Gondwana Land (presently a part of Chattishgarh, Madhya Pradesh, Andhra Pradesh and Mahaarastra state). Subsequently the mixture and merger of these three waves of people occurred with the passage of time.

The present study was undertaken with the objective to study the prevalence of hemoglobinopathies and characterize the molecular heterogeneity of Sickle Cell Disease and correlate the phenotype with various genotypes.

**Sβ-Thalassemia in Western Orissa:**

In the present study 60 cases of Sβ-thalassemia satisfying the inclusion criteria were confirmed by ARMS PCR for the diagnosis of associated β-thalassemia mutations. The incidence of Sβ-thalassemia in the Western Orissa population was found to be 9.6% among the SCD patients. Our finding is similar to the earlier studies of this population conducted by Kar (1991).

A hospital based study in Western Mahaarastra noted 3.6% cases (1.8% each from Sβ⁰ thalassemia and Sβ⁺ thalassemia) of Sβ-thalassemia (Ambedkar et al. 2001). However another
hospital based study in North Karnataka found a lone case of Sβ-thalassemia in 50 hemoglobinopathies cases (Shivshankar et al, 2008).

Earlier, it has been estimated that Sβ° thalassemia occurs approximately once in every 23000 Afro-Americans (Steinberg & Dreiling 1976) and Serjeant et al, (1979) observed a frequency of 1: 6750 in Jamaica population.

Our study reveals all cases of Sβ-thalassemia had one β-thalassemia mutation i.e. IVS1-5(G→C). This observation is similar to the earlier findings (Donaldson et al, 2000 and Chhotray et al, 2004). IVS1-5(G→C) is the commonest β-thalassemia mutation observed in India (Verma et al, 1997, Bandopadhaya et al, 1998). However, study by Ambedkar et al, (2001) observed both IVS1-5(G→C) and cd 41/42 mutations in equal percentage (50%) among the Sβ-thalassemia cases.

In our study population the HbA% ranged from (3-7) %. Kulozik et al, (1991) had assumed the HbA% to be (3-5) % in the Sβ+ thalassemia cases studied in this region by observing HbA band in cellulose acetate electrophoresis. Donaldson et al, (2000) noted Sβ+ Thalassemia patients with IVS1-5(G→C) mutation had variable HbA% with average 5.6%. Ambedkar et al. (2001) found 19.8% of HbA (average) in Sβ+ thalassemia associated with IVS1→5 (G→C) mutation.

Serjeant and his co-worker (2001) reported that Sβ+ thalassemia type-I is severe defect associated with 3-5% HbA most commonly in Indian patients; type-II has higher level of HbA (5-18) % and occurs around the Mediterranean whereas type-III has (18-25%) HbA runs a mild course and is the type most frequently seen in patients of African origin. In the present study 75% cases had Sβ+ thalassemia type-I (HbA-3-5%) and 25% cases were Sβ+ thalassemia type-II
(HbA>5%). This finding is consistent with the earlier reports from Western India (Ambedkar et al, 2001) and Jamaica (Donaldson et al, 2000).

**Epidemiology:**

Among 60 patients of Sβ⁺ thalassemia 73% were male and 27% were female. Majority of the patients enrolled were in the age group of 11-30 years in both Sβ⁺ thalassemia type-I and type-II. The mean age was 22.4 ± 9.7 years, the eldest patient enrolled was of 51 years age and 2% cases were above the age of 50 years. Similar findings were observed by Kulozik et al, (1991) in the same population. Preponderance of male may be due to social customs taking more care of male children or disproportionate hospital admission between males and females.

Our finding suggests that 2/3rd of Sβ⁺ thalassemia (both type-I and type-II) patients belong to non tribal population. This finding is similar to the earlier study from this population (Kar 1991).

**Comparison between Sβ⁺ Thalassemia type-I and type-II:**

In the present work we have studied clinical features and hematological indices of both Sβ⁺ thalassemia type-I and type-II in detail. No other cohort or community study has been done earlier in this country for comparison to give an overall picture regarding clinical features and hematological indices in these above groups. However significant comparison could not be done in the said groups regarding many clinical features because of small no. of cases in the present study.

Painful crisis was found to be the commonest clinical presentation in this study. Incidence of painful crisis was significantly higher in the Sβ⁺ thalassemia type-I (93.3%) than
type-II (66.6%) as evident by Fisher exact test (P<0.05). However, frequency of painful crisis was not different statistically in both the groups. Transfusion dependent anemia was found in 62.2% of Sβ⁺ thalassemia type-I which is high in comparison to type-II (53.3%). Higher frequency of transfusion was observed 0.3±0.6 in the earlier group in comparison to the later (0.08±0.14). Splenomegaly (73%) and splenic atrophy (6%) were found to be more in Sβ⁺ thalassemia type-II comparatively. However other clinical features were observed to be similar in both the groups.

Study by Serjeant et al. (1982) observed that Sβ⁰ thalassemia had significantly high hospitalisations for painful crisis, splenectomy, hepatomegaly and early menarche in comparison to Sβ⁺ thalassemia in Jamaica.

In this study all the hematological indices (total Hb, RBC count, MCV, MCH, MCHC, HbF, and HbS) were found to be similar in both groups except HbA₂. Study from Jamaica noted significantly more HbA₂ and HbF and less Hb, RBC count, MCV and MCHC in Sβ⁰ thalassemia in comparison to Sβ⁺ thalassemia group (Serjeant et al. 1982).

**Molecular Characterization of Sβ⁺ Thalassemia:**

Among 60 Sβ⁺ thalassemia cases 96% β⁸ chromosome were found to be linked to Asian haplotype (+++-----) and 4% were atypical. Present findings are not similar to the earlier study of Kulozik et al. (1991) from the same population. They observed Asian haplotype in all the β⁸ chromosomes. The variation may be due to inclusion of less number of cases in that study.

β⁺Thal chromosomes were found to be linked with multiple (9 different types) haplotype. Forty two percent (42%) had (+-----+), 36% had (-------+), 12% had (-------). Rest of the 10% had
mixture of different haplotypes. Whereas Kulozik et al, (1991) found only three different types of haplotype in $\beta^{thal}$ chromosomes.

The predominant $\beta^{thal}$ haplotype (+-----+) in this study is consistent with earlier findings from India. Study by Varawalla et al, (1992) observed $\beta^{thal}$ haplotype (+-----+) in the population of Gujarat, Punjab, Sindh and North West Pakistan (both in the thalassemia and normal population). Same finding was seen by Bandyopadhaya et al (1999) in eastern India population, by Venkatesan et al, (1992) in Southern India and Gupta et al, (2008) in the hospitalized population (cases from Uttar Pradesh, West Bengal and Gujarat) of Uttar Pradesh. In Gujarat and Sindh (+-----+) haplotype was predominantly associated with IVS 1-5(G→C) and 619 base pairs deletion.

The 2nd predominant $\beta^{thal}$ haplotype (------+) of our study was found to be rare and associated to IVS 1-5(G→C) (Varawalla et al, 1992). A study by Gupta et al, (2008) found the said haplotype in Uttar Pradesh (3 cases) and Gujarat (1 case) were associated with $\beta$-thalassemia mutation IVS 1-5(G→C).

In our study the type-VII haplotype (-+-++++) was common to both $\beta^s$ chromosome (4%) and $\beta^{thal}$ chromosome (2%). Similar haplotype was found to be associated to cd 41/42 $\beta$-thalassemia mutation in earlier studies (Kazzazian et al, 1984, Varawalla et al, 1992) and HbE-codon 26(G→A) (Bandyopadhaya et al, 1999).

The great diversity of haplotypes associated with IVS1-5(G→C) mutation, its high frequency and widespread distribution suggest that it may be the oldest $\beta$-thalassemia mutation in the Indian subcontinent.
No significant difference was observed in clinical features inspite of different $\beta^{Thal}$ haplotype in $S\beta^+$ thalassemia. Influence of haplotype on any of the phenotypic manifestations of the disease was not observed although transfusion dependent anemia, splenomegaly, hepatomegaly were less in the type-II group. It may be due to few no. of cases in both the above group.

Significantly more HbA%, HbA$_2$% and lower MCH, MCHC was observed in the type-II group ($p < 0.05$). The $\beta^{Thal}$ haplotype-II appeared to be better clinically and hematologically in comparison to $\beta^{Thal}$ haplotype -III in $S\beta^+$ thalassemia of our population. No study has been done earlier in any population to analyse the influence of $\beta^{Thal}$ haplotype in $S\beta$ Thalassemia.

**$\alpha$-Thalassemia in $S\beta^+$ Thalassemia:**

In the present study 41 cases of $S\beta^+$ thalassemia type-I and 14 cases of type-II were amplified and studied for the co-inheritance of $\alpha$-thalassemia. The $S\beta^+$ thalassemia type-I had heterozygous 3.7 $\alpha$-thalassemia ($\alpha\alpha/-\alpha 3.7$) in 11 (26.8%) cases, heterozygous 4.2 $\alpha$-thalassemia ($\alpha\alpha/-\alpha 4.2$) in a lone case and none with homozygous $\alpha$-deletion. In the $S\beta^+$ thalassemia type-II 2 cases had (13.3%) heterozygous 3.7 $\alpha$-thalassemia ($\alpha\alpha/-\alpha 3.7$) and a lone case had homozygous 3.7 $\alpha$-thalassemia (-$\alpha$ 3.7/-$\alpha$ 3.7). Influence of heterozygous 3.7 $\alpha$-thalassemia ($\alpha\alpha/-\alpha 3.7$) upon clinical features and hematological indices was studied further in $S\beta^+$ thalassemia type-I only. The effect of other $\alpha$-thalassemia deletion on the $S\beta^+$ thalassemia type-I and type-II could not be studied because of small no. of cases.

Kulozik et al, (1991) observed normal $\alpha$ globin genotype in 7 cases, heterozygous $\alpha^+$ thalassemia in 4 cases and $\alpha^+$ homozygous thalassemia in 6 cases out of 17 cases of $S\beta^+$ thalassemia giving an $\alpha^+$ thalassemia gene frequency of 0.47. The $\alpha^+$ deletions were rightward
(3.7 kb) type in 7 cases and of the leftward (4.2 kb) type in 9 cases. They could not study the influence of said α-thalassemia because of small numbers of patients.

The clinical severity was similar in both the Sβ⁺ thalassemia type-I with heterozygous 3.7 α-thalassemia (αα/-α3.7) and Sβ⁺ thalassemia type-I without α-thalassemia. However, frequency of total hospitalization was found to be significantly more (p<0.05) in the Sβ⁺ thalassemia type-I with heterozygous 3.7 α-thalassemia (αα/-α3.7) (3.4 ± 6.6) in comparison to Sβ⁺ thalassemia type-I without α-thalassemia (0.3 ± 0.5).

Significant increase in HbA₂, HbF and low HbS (p<0.05) was observed in the Sβ⁺ thalassemia type-I without α-thalassemia. Our finding is dissimilar to the earlier findings of Ballas et al. (1997). In the present study a single case was observed with homozygous 3.7 α-thalassemia having MCV-69fl and HbA₂ 6.7%. This observation is similar to the earlier publication of Ballas et al. (1997) that Sβ⁰ thal with two alpha gene deletion (-α/-α) had an MCV less than 70fl and HbA₂ = 6.0%.

There is strong evidence that α- thalassemia modulates the hematological and clinical features of β-thalassemia (Steinberg et al, 1984) but there are very few studies regarding effect of α-thalassemia upon Sβ⁻ thalassemia because of rarity of this compound heterozygote.

Steinberg and his co-workers (1984) observed the effect of both homo and heterozygous α⁺ thalassemia upon Sβ⁰ thalassemia. Patients with Sβ⁰ thalassemia with α⁺ thalassemia closely resembled with Sβ⁰ thalassemia except for balanced globin synthesis ratios and lower HbF level. Cases of Sβ⁰ thal with homozygous α-thalassemia had less MCV, decreased frequency of acute chest syndrome and painful crisis in comparison to Sβ⁰ cases with heterozygous α-thalassemia.
Another study by Vyas et al., (1988) observed $\alpha^0$ thalassemia with $\alpha$-thalassemia had significantly higher Hb levels and lower reticulocyte counts independent of the presence of splenomegaly. Splenomegaly at age of 5 years and episodes of acute splenic sequestration was significantly more frequent in $\alpha^0$ cases with normal $\alpha$ globin gene status. There were no significant differences in painful crises, acute chest syndrome or other clinical features.

**Comparison between $\beta^+$ Thalassemia type I, $\beta^+$ Thalassemia type II and SCD:**

In this present study $\beta^+$ thalassemia type I cases had significantly more incidences of painful crisis ($x^2$=7.1, $p<0.02$) in comparison to $\beta^+$ thalassemia type II and SCD. But frequency of painful crisis was observed to be more than SCD only ($p<0.05$). However other clinical features were similar in all the groups. Because of small no. of patients in the $\beta^+$ thalassemia type-II group it was not possible to compare the clinical features with $\beta^+$ thalassemia type I and SCD.

Kulozik et al., (1991) observed that clinical features of $\beta^+$ thalassemia did not differ from SCD significantly in this population. Persistent splenomegaly was found in 66% of SCD and 82% in $\beta^+$ thalassemia. Attacks of splenic pain were reported in 24% of $\beta^+$ thalassemia and 15% with SCD although multiple admissions for pain were more common in the later group. In our study splenomegaly was found to be more in both $\beta^+$ thalassemia type-I (66%) and type-II (73%) in comparison to SCD (52%). Persistent splenomegaly and gross splenic enlargement are peculiarities of SCD in India and recurrent malaria is one of the causes of persistent splenomegaly. Significant difference was not obtained because of few numbers of cases in $\beta^+$ thalassemia type-II.
Another study by Kar (1991) from the same population observed similar incidence of painful crisis, splenic sequestration, hepatic sequestration, anemia, hand-foot syndrome in SCD patients and Sβ-thalassemia cases. However repeated pain attacks, splenic pain and bone necrosis were found to be significantly more in Sβ-thalassemia than SCD patients.

Serjeant et al, (1979) found that splenomegaly and splenectomy were significantly higher in Sβ Thalassemia than SCD whereas other clinical features (i.e. painful crisis, leg ulcer, pneumonia, aplastic crisis) were similar.

Zago et al, (1980) observed that the incidence of splenomegaly is more in Sβ° thalassemia in comparison to SCD. However other complications like joint pains, abdominal pains, hospitalization for pain, pneumonia, leg ulcer and hepatomegaly were similar in both the groups.

Platt et al, (1991) found that in SCD the average rate of painful crisis was 0.8 episode per patients-year, 1.0 episode per patient-year in Sβ° thalassemia and 0.4 episode per patient-year in Sβ° thalassemia.

However some patients in both Sβ° thalassemia type-I and type-II (4% and 6%) had regressed spleen which was observed during follow up suggesting that fibrosis of spleen may occur in Sβ° thalassemia as well, although less commonly than SCD (13%). This finding is similar to the earlier documentations of Zago et al, (1980)

Sβ° thalassemia cases (both type-I and type-II) had significantly less MCV, MCH and more HbA2 (p<0.05) in comparison to SCD. However the HbF % was significantly more in SCD in comparison to Sβ° thalassemia type-I only (p<0.05) although moderately elevated in both the group. It could be due to presence of Asian haplotype and in both the β° chromosome of SCD
and Xmn-I polymorphism. Our findings are similar to the observations of Kulozik et al., (1991) that patients with Sβ+ thalassemia had significantly higher values of HbA2 and lower values of MCV and MCHC compared to those with SCD but other indices did not differ significantly between genotypes.

Another study by Serjeant et al., (1979) found significantly higher Hb, HbA2, HCT, RBC count and lower MCV and MCH in Sβ0 thalassemia than SCD. Same author (1982) observed significantly more HbA2, HbF, reticulocyte and less Hb, RBC count, MCV in Sβ0 thalassemia in comparison to Sβ+ thalassemia.

Zago et al., (1980) observed lower MCV, MCH and higher HbA2 in Sβ0 thalassemia than SCD. Total Hb level was slightly lower in SCD but the difference was not significant. HbF was moderately elevated to similar levels in both groups. However, study by Balias et al., (1997) found only low MCV and higher HbA2 in Sβ-thalassemia in comparison to SCD.

In our study no significant difference was observed in all the clinical features (pain rate, transfusion rate, splenomegaly, hepatomegaly, cholelithiasis) except frequency of hospitalisations among Sβ+ thalassemia type-I with heterozygous 3.7 α-thalassemia (αα/-α3.7) and in SCD with heterozygous 3.7 α-thalassemia (αα/-α3.7). Because of small no. of cases statistically significant difference was not observed in many clinical features. The frequency of hospitalization was significantly more in Sβ+ thalassemia type-I with heterozygous 3.7 α-thalassemia (αα/-α3.7) 3.4±6.6 in comparison to SCD with heterozygous 3.7 α-thalassemia (αα/-α3.7) 0.1±0.1 (p<0.05).

Although complain of painful crisis was similar in both the groups, only 27.2% of Sβ+ thalassemia type-I with heterozygous 3.7 α-thalassemia (αα/-α3.7) had history of hospitalization
for painful crisis. It may be due to mild painful crisis not requiring hospitalization supported by microcytosis (MCV 68.02±4.3) and lower HbS concentration (67.4±9.12) %.

In a multicentric study conducted in USA Steinberg and co workers (1984) depicted lower frequency of painful episode, aseptic necrosis, acute chest syndrome and more leg ulcer in Sβ⁰ thalassemia with heterozygous α-thalassemia (-α/αα) in comparison to SCD with heterozygous α-thalassemia (-α/αα). No test for significance was done in this study.

Sβ⁺ thalassemia type-I with heterozygous 3.7 α-thalassemia (αα/-α3.7) cases had significantly less MCV, MCH, HbS and more HbA₂ (p<0.05) in comparison to SCD with heterozygous 3.7 α-thalassemia (αα/-α3.7). Similar observations were noted by Steinberg et al. (1984). They observed lower MCV and higher HbA₂ in Sβ⁰ thalassemia with heterozygous α-thalassemia (-α/αα) in comparison to SCD with heterozygous α-thalassemia (-α/αα) whereas the Hb and HbF were similar. There was no test for significance in the above study. Similar observations were demonstrated by Ballas et al, (1997). The modulating role of αβ-thalassemia (different combinations) in phenotypic expression of SCD should be carried out in a larger population.

α-Thalassemia in Homozygous SCD:

Epidemiology:

Of 300 SCD cases satisfying the inclusion criteria for study of β-globin cluster haplotype, 267 cases were amplified for α globin gene. Amongst them 199 cases (74.5%) had a normal α genotype (αα/αα), whereas 68 cases (25.5 %) had α-thalassemia. This finding is consistent with the earlier publications. Kar et al, (1986) observed the frequency of α-gene in Indian SCD
patients to be 0.317. Kulozik *et al*, (1988) noted the overall frequency of \( \alpha \)-thalassemia to be 0.29 in this population. Another study by Mishra *et al*, (1991) had observed 12.6% of \( \alpha \)-thalassemia in Orissa population.

\( \alpha \)-thalassemia was found to be much higher in general population of West Central Gujarat (95%) and Nilgiri hills in South India (87.5%) suggesting that the condition is almost genetically fixed in India (Labie *et al*, 1989). Another study conducted by Sarkar *et al*, (2006) noted the allele frequency for \( \alpha \)-thalassemia to be 0.09 in a hospitalized population (non-tribal) of North India. Alpha genotyping performed in various tribal and non-tribal populations showed frequency rates ranging from 18 to 96% in various studies (Desai 1997). However, the frequency of \( \alpha \)-thalassemia was found to be low (0.185%) in the SCD population of Jamaica in comparison to SCD population of India (Kar *et al*, 1986).

In our study, 57 SCD cases (21.3%) had heterozygous 3.7 \( \alpha \)-thalassemia (\( \alpha \alpha/-\alpha 3.7 \)), 3 cases (1%) had heterozygous 4.2 \( \alpha \)-thalassemia (\( \alpha \alpha/-\alpha 4.2 \)) and 8 cases (3%) had homozygous 3.7 \( \alpha \)-thalassemia (\( -\alpha 3.7/-\alpha 3.7 \)). Heterozygous \( \alpha \)-thalassemia single gene deletion was the commonest \( \alpha \)-thalassemia found in 22.3% followed by homozygous \( \alpha \)-thalassemia (3%) in SCD. This finding is dissimilar to the previous observations from this population. Kar (1991) found 42.85% heterozygous \( \alpha \)-thalassemia and 10.31% homozygous \( \alpha \)-thalassemia in SCD of this population.

The prevalence of heterozygous and homozygous \( \alpha \)-thalassemia was found to be \( \approx 30\% \) and 4% respectively in SCD patients of Jamaica (Stevens *et al*, 1986). Pediatrics population from Guadeloupe showed 40.7% of heterozygous \( \alpha \)-thalassemia and 3.3% homozygous \( \alpha \)-thalassemia in SCD.
Present study shows that $-\alpha^{3.7}$ deletion (24.3%) is the predominant mutation in SCD. Similar findings were noted earlier from this population by Kulozik et al, (1987). The overall frequency of $\alpha^{3.7}$ deletion was found to be 16.25% in the eastern population of India (Sarkar 2005). Same author noted 30.8% heterozygous 3.7 α-thalassemia in a hospitalized population of North India (Sarkar et al, 2006). $-\alpha^{3.7}$ deletion was observed to be the commonest mutation in most of the studies (Africa, Greece, Spain, Sicily, Thailand and Australia) all over the world (Weather et al. 2001).

Of the 68 SCD with α-thalassemia cases, 43 (62%) were male and 25 (37%) were female. Majority of the patients (38.2%) were in the age group of 21-30 yrs. The mean age was 23.6 ± 10.3 Yrs. Kulozik et al, (1987) reported that α-thalassemia was more common in SCD patients 10 years old or older than younger patients. The significantly greater α gene frequency found among older patients may delay the onset of symptoms and has a positive effect on survival of patients. However, present study did not find any correlation between α-thalassemia and survival of patients in SCD although 88% cases were above 10 years of age in SCD with α-thalassemia.

Fifty two (52) cases in our study (76.4%) were nontribal Hindus and 14 cases (20.5%) were tribal Hindu. This finding is dissimilar to the previous report of Mukherjee et al, (1997) who found prevalence of α-thalassemia was more in the tribal (85.8%) population in comparison to non-tribals (13.3%). The allele frequency of $-\alpha^{3.7}$ gene in a central India based tribal population was found to be more (0.65) than non-tribal (0.07-0.12) (Gupta 1991).
Alpha thalassemia is more prevalent in certain caste Hindus like Kuilta, Chassa, Gouda in our population which could be due to consanguineous marriages which is a common social practice in this caste.

**Influence of α-Thalassemia in Phenotypic Expression of Homozygous SCD:**

Influence of heterozygous 3.7 α-thalassemia, homozygous 3.7 α-thalassemia and heterozygous 4.2 α-thalassemia (αα/-α 3.7, -α 3.7/-α 3.7 and αα/-α 4.2) on SCD patients were studied in detail. Several published studies have ignored the influence of heterozygous α-thalassemia upon SCD. The effect of α-thalassemia on sickle red cells are well known but the role of heterozygous α-thalassemia single gene deletion had not been studied due to minimal effect on the pathophysiology of SCD. However the present study elucidates the effect of heterozygous α-thalassemia (αα/-α 3.7) upon SCD in this population.

In the present study painful crisis was the commonest clinical presentation. The frequency of painful crisis (VOC>2ep/yr) was observed less in SCD patients with both hetero and homozygous 3.7 α-thalassemia (αα/-α 3.7 and -α 3.7/-α 3.7) in comparison to SCD without α-thal ($\chi^2$-12.5, $p<0.006$). Other clinical features were found to be similar in all the three groups of SCD with α-thalassemia (heterozygous 3.7 α-thalassemia, homozygous 3.7 α-thalassemia and heterozygous 4.2 α-thalassemia) and without α-thalassemia. This observation is similar to the earlier findings by Mukherjee et al, (1998) in Western India. They noted that the clinical presentation in SCD patients with α-thalassemia were milder with few episodes of painful crisis, chest syndromes, infection, requirement of hospitalization and blood transfusion. However, the impact of α-thalassemia on the clinical severity of SCD was not convincingly demonstrated in Orissa (Kar et al, 1986, Kulozik et al, 1987).
Higher incidence of acute painful episodes in SCD with \( \alpha \)-thalassemia was reported by Billet \textit{et al}, (1995). Ballas \textit{et al}, (2001) in USA observed that SCD with homozygous \( \alpha \)-thal increased prevalence of avascular necrosis, retinopathy and splenomegaly, but decreased prevalence of leg ulcers and cerebro vascular accidents.

Study conducted by Higgs \textit{et al}, (1982) in Jamaica population found SCD with homozygous \( \alpha \)-thalassemia-2 had fewer episodes of acute chest syndrome and chronic leg ulceration and more patients had splenomegaly as compared to SCD without \( \alpha \)-thalassemia.

Steinberg \textit{et al}, (1984) did not find any significant role of \( \alpha \)-thalassemia in amelioration of vasoocclusive complications in SCD. However, SCD patients with \( \alpha \)-thalassemia were observed to have a greater prevalence of aseptic necrosis of bone and incidence of acute chest syndrome. Natta (1978) suggested that \( \alpha \)-thal has no role in the modulation of clinical severity in SCD.

In all the three groups of SCD with heterozygous 3.7 \( \alpha \)-thalassemia, homozygous 3.7 \( \alpha \)-thalassemia and heterozygous 4.2 \( \alpha \)-thalassemia (\( \alpha \alpha/-\alpha 3.7 \),\(-\alpha 3.7 \)/\(-\alpha 3.7 \) and \( \alpha \alpha/-\alpha 4.2 \)) patients had significantly lower MCV, MCH and higher RBC count (\( p < 0.05 \)) as compared to SCD without \( \alpha \)-thalassemia (\( \alpha \alpha/\alpha \alpha \)). This finding is similar to the earlier observations from this population (Kulozik \textit{et al}. 1987). Similar observations were also documented by Mukherjee \textit{et al}. (1998).

Higgs \textit{et al}. (1982) observed SCD patients with alpha thalassemia-2 had significantly higher red cell count, Hb, HbA2 as well as significantly lower HbF, MCH, MCV than those with a normal \( \alpha \) globin gene component.
Stevens et al, (1986) in pediatrics population of Jamaica observed significant lower MCV, higher red cell counts, higher HbA$_2$ level in SCD with α-thalassemia than SCD without α-thalassemia.

Another investigation in black population by Steinberg and Embury (1986) noted comparatively lower MCV and higher Hb and HbA$_2$ in SCD with α-thalassemia.