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# ORAL ABSTRACTS

## 114.SICKLE CELL DISEASE, SICKLE CELL TRAIT AND OTHER HEMOGLOBINOPATHIES, EXCLUDING THALASSEMIAS: CLINICAL AND EPIDEMIOLOGICAL

### Sickle Cell Trait As a Risk Factor for Leukemia: A Nationwide Study

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**INTRODUCTION:**
Leukemia is a cancer of blood-forming cells. It can arise from cells of lymphoid or myeloid lineage. It can arise from genetic mutations in tumor suppressor genes, proto-oncogenes or both. It affects over two million people worldwide. A combination of genetic factors and extrinsic factors are believed to play a role. Sickle cell disease (SCD), an inherited disorder leading to the formation of abnormal hemoglobin (HbS) and red blood cell sickling, has been shown to increase the risk for leukemia, presumably due to an increased bone marrow turnover rate. We aimed to explore if sickle cell trait (SCT), when people inherit only one of the two sickle cell genes, is associated with an increased risk for leukemia.

**METHODS:**
In this case-control study, we evaluated an association between leukemia (and its subtypes) and SCT in a nationwide cohort of hospitalized patients included in the National Inpatient Sample (NIS) 2016-2019 database. The inclusion criteria for cases were patients who had any of the following ICD-10-CM codes for leukemia: C91 (lymphoid leukemia), C92 (myeloid leukemia), C93 (monocytic leukemia), C94 (other leukemia of specified cell type), and C95 (leukemia of unspecified cell type). The exclusion criteria were Down syndrome (Q90), Fanconi anemia (D61.09), ataxia-telangiectasia (G11.3), Bloom syndrome (Q82), myelodysplastic syndrome (D46), lymphoma (C81, 85), and solid malignancies (C00-75) as these diseases and/or their treatments are known to increase the risk for leukemia independently of SCT (ICD-10-CM D57.3). The controls included patients in the NIS database who do not have the ICD-10-CM codes for leukemia and meet the exclusion criteria applied to the cases. For each year, we used a 1:4 propensity score matching routine. Our match variables were sex, the six race categories used by NIS, and 11 age groups. Four perfect matches (controls) were identified for each case ('any leukemia' diagnosis). Patient characteristics were compared using Pearson chi-squared test. Odds ratios (ORs) were calculated for 'any leukemia' diagnosis, as well as for each subtype of leukemia. Five multivariate logistic regression models were used to examine the relationship between the leukemia subtypes and SCT while controlling for age group, sex, and race.

**RESULTS:**
We identified 181,676 cases and 726,704 controls. The mean age of subjects was 59 years. The majority of subjects (56%) were male. A greater proportion of patients with SCT were found among cases (0.12%) compared to controls (0.08%) ($p < 0.0001$). The OR for 'any leukemia' was 1.48 (95% CI 1.27-1.73, $p < 0.0001$). When the association between SCT and specific subtypes of leukemia was evaluated, it was statistically significant for myeloid and monocytic leukemias, OR 1.74 (95% CI 1.40 - 2.17) and 2.20 (95% CI 1.09 - 4.42) correspondingly.

**CONCLUSION:**
Our case-control study revealed statistically significantly higher odds of SCT among patients with any leukemia (and specifically myeloid and monocytic leukemias) as compared to controls which can be postulated to the common myeloid progenitor lineage of erythrocytes. Our results suggest that, similarly to SCD, SCT although a benign condition can increase the risk for leukemia. To better understand this association, future prospective studies are needed for the mapping of individual risk factors and examining the HbS% levels in SCT carriers who go on to develop leukemia.

**Disclosures** No relevant conflicts of interest to declare.

| | Leukemia (any type) | | | |
|---|---|---|---|---|
| Sickle Cell Trait, n (%) | Yes, n (%) | No, n (%) | P-value | OR (95% CI) |
| Yes | 221 (0.12) | 597 (0.08) | <0.0001 | 1.48 (1.27, 1.73) |
| No | 181455 (99.88) | 726107 (99.92) | | |
| | Lymphoid Leukemia (C 91) | | | |
| Sickle Cell Trait, n (%) | Yes, n (%) | No, n (%) | P-value | OR (95% CI) |
| Yes | 96 (0.01) | 597 (0.08) | 0.05 | 1.24 (1.0, 1.54) |
| No | 94182 (99.9) | 726107 (99.92) | | |
| | Myeloid Leukemia (C 92) | | | |
| Sickle Cell Trait, n (%) | Yes, n (%) | No, n (%) | P-value | OR (95% CI) |
| Yes | 93 (0.14) | 597 (0.08) | <0.0001 | 1.74 (1.40, 2.17) |
| No | 64934 (99.86) | 726107 (99.92) | | |
| | Monocytic Leukemia (C 93) | | | |
| Sickle Cell Trait, n (%) | Yes, n (%) | No, n (%) | P-value | OR (95% CI) |
| Yes | 8 (0.18) | 597 (0.08) | 0.02 | 2.20 (1.09, 4.42) |
| No | 4430 (99.82) | 726107 (99.92) | | |
| | Other Leukemia of specified cell type (C 94) | | | |
| Sickle Cell Trait, n (%) | Yes, n (%) | No, n (%) | P-value | OR (95% CI) |
| Yes | 11 (0.14) | 597 (0.08) | 0.09 | 1.66 (0.92, 3.02) |
| No | 8041 (99.86) | 726107 (99.92) | | |
| | Leukemia of unspecified cell type (C 95) | | | |
| Sickle Cell Trait, n (%) | Yes, n (%) | No, n (%) | P-value | OR (95% CI) |
| Yes | 9 (0.12) | 597 (0.08) | 0.29 | 1.43 (0.74, 2.76) |
| No | 7657 (99.88) | 726107 (99.92) | | |

**Figure 1**

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