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Status of Anemia and Haemoglobinopathies in Kumaun Region, Uttarakhand, India

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Abstract: The objective of the present study was to evaluate the status of anemia and haemoglobinopathies in Kumaun Region, India. An extensive survey was conducted to collect the data from various sources like government hospitals, Primary Health Centre's, Certified Pathology labs and the medical registry maintained by related Government Departments. During the investigation, the maximum number of Anemia, thalassemia trait, SC β T, SCT, Sickle cell anemia (SCA)/Sickle cell disease (SCD) and thalassemia major cases were recorded from the district Udham Singh Nagar followed by Nainital and minimum cases were reported from two mountain districts Bageshwar and Champawat.

Keywords: Anemia, Sickle cell anemia, Haemoglobinopathies, β Thalassemia, Kumaun Region

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Introduction

Sickle cell anemia (SCA) develops due to a single base substitution in the β -globin gene. Sickle cell disease (SCD) is primarily diagnosed through hematological techniques to analyze structural deformities in red blood corpuscles. Sickle cell disease is a condition when red blood corpuscles cohort into a sickle shape (Melkani, 2020). Sickle cell anemia is the rapidly increasing chronic disorder globally and in India has the second-highest burden of the disease (Hockman *et al.*, 2018). A single nucleotide substitution causes SCA at position 6 of the β -globin gene; its pathophysiology stems from the polymerization of the resulting sickle hemoglobin variant (HbS),

triggering a cascade of erythrocyte alterations (Odievre *et al.*, 2011; Ware *et al.*, 2017). Individuals with SCA experience considerable morbidity from both acute and chronic sequelae. This disease can be fatal in the lack of effective treatment even within the first few years of life (Piel *et al.*, 2017). SCD gets transmitted through the autosomal recessive mode of inheritance. Two copies of HbS may combine (SS disease), or one copy of HbS and another β -globin variant, such as HbC, may combine (double heterozygous SC disease). Individuals with one copy of HbA and one copy of HbS have the sickle-cell trait, the carrier state for

SCD. β -thalassemia occurs when a reduced amount of β -globin is present. This condition is beta-plus (β^+) thalassemia, whereas the absence of β -globin is beta-zero (β^0). Either of these conditions may combine with HbS, leading to a compound heterozygous state (Elagouz *et al.*, 2010).

Nearly one-third of the world's population is suffering from anemia due to various causes (Ratre *et al.*, 2004; McLean *et al.*, 2009; Milman, 2011; Khambalia *et al.*, 2011; Mauricio *et al.*, 2013). In India, prevalence is very high as compared to world prevalence (Kalaivani, 2009; Prakash, 2011). The overall literacy among scheduled castes (SC) is 74.41%, and scheduled tribes (ST) is 73.88% compared to the state average of 78.80%. It indicates the level of educational similarity among the SC and ST population in Uttarakhand. Tribes of Uttarakhand mainly comprise five major groups-- the Jaunsari tribe, Tharu tribe, Raji tribe, Buksa tribe, and Bhotiyas. In terms of population, the Jaunsari tribe is the most significant tribal group of the state.

Anemia is a nutrition deficient disease globally. According to the National Family Health Survey 4 (NFHS-4), 58.4% of children aged 6–59 months, 53.1% of non-pregnant women aged 15–49 years, 50.3% of pregnant women aged 15–49 years, 53% of all women aged 15–49 years, 22.7% of men aged 15–49 years, 54% of adolescent girls and 29% boys are anemic in India (Kishore *et al.*, 2020). According to UNICEF report, more than half of Indian women, including pregnant and lactating mothers, are anemic.

Hemoglobinopathies are inherited structural disorders of hemoglobin. Approximately 1000 types of Hemoglobinopathies have been documented, out of which, most of them are asymptomatic and other prominent hemoglobinopathies are Thalassemias (both α and β), Sickling disorders (Hb SS, Hb SC, Hb SD, Hb SO), Cyanosis (such as Hb Kansas), Hemolytic anemias (such as Hb H) and Erythrocytosis (such as Hb Malmo).

Approximately 5% people of the world's population are the carrier of hemoglobin disorders. Hemoglobinopathies affect approximately 370,000 newborn babies each year in the world. The hemoglobin variants of most clinical significance are hemoglobin S, C, and E. In West Africa, approximately 25% of individuals are heterozygous for the hemoglobin S (Hb S) gene related to sickle cell diseases. In addition to the above high frequencies of Hb S gene alleles were reported from Caribbean, South and Central Africa, Mediterranean, Arabian Peninsula and India.

Hemoglobin C (HbC) is found primarily in people living or originating from West Africa. Hemoglobin E (Hb E) is found in Asia, with the highest prevalence rate from Thailand. β -thalassemia cases are reported from the Mediterranean, Arabian Peninsula, Turkey, Iran, West and Central Africa, India and other Southeast Asian countries, whereas the α -thalassemia is typical in many parts of Africa, Mediterranean, Middle East, and throughout Southeast Asia (Rappaport *et al.*, 2004) (Fig. 1). The common β -chain defect hemoglobinopathies are HbS (seen most often in African Americans), HbC (seen most often in African Americans), HbE (seen most often in SE Asians) and the common α -chain defect is Hb G (seen most often in African Americans). The common δ -chain defect is HbA2' (seen most often in African Americans).

Materials and Methods

Extensive survey was made to collect data from various Primary Health Centre's, Certified Pathology labs and district hospitals of Kumaun Region (Fig. 2) and analyzed the current status of anemia, thalassemia trait and variants, sickle cell β thalassemia and thalassemia major.

Results

The present study revealed that most of the cases of hemoglobinopathies are present in Udham Singh Nagar, followed by Nainital, Pithoragarh, Almora, Champawat, and Bageshwar. The number

Fig. 1: Presence of Sickle Cell Anemia in India (Colah *et al.*, 2015).

Fig. 2: Districts of Uttarakhand, Kumaun Region.

Table 1: Number of cases reported from all districts of Uttarakhand

	Anemia	Thalassemia Trait	SC β T	SCT	SCA/SCD	Thalassemia Major
Champawat	239	232	0	2	0	30
Bageshwar	191	186	0	2	0	24
Nainital	956	931	2	9	1	121
Udham Singh Nagar	1434	1396	3	13	2	181
Almora	478	465	1	4	0	60
Pithoragarh	573	558	1	6	0	72

Fig. 3: Graphical representation of number of cases.

of Anemia cases reported from various districts have been shown in Table 1 and Figure 3.

Discussion

Sickle cell disease (SCD) is one of the most common inherited single-gene disorders. Polymerization of sickle hemoglobin results in inflexible and adherent erythrocytes, leading to coagulation, vascular and cellular activation, and resultant blood vessel blockage.

The primary defect in SCD involves the erythroid lineage and results in two significant abnormalities, enhanced red cell destruction (hemolysis) with the corresponding reticulocytosis (Smith *et al.*, 2021).

Foetal hemoglobin (HbF) induction to treat β -hemoglobinopathies and HbF induction in β -thalassemia could overcome ineffective

hematopoiesis and thus terminates transfusion dependency for formerly transfusion-dependent patients (Eltaweel, 2021). Sciano (2021) provided a diagnostic tool Eva-BeTa for identifying ancient individuals affected by β -thalassemia for genetic confirmation. Pathophysiology of β -thalassemia addition to crucial developments in optimizing transfusion programs and iron-chelation therapy has led to an increase in the life span of thalassemia patients. These patients are classified into three categories based on their different features of the underlying pathophysiology of β -thalassemia-- correction of the globin chain imbalance, addressing ineffective erythropoiesis, and improving iron overload (Motta *et al.*, 2020). A new era of novel therapies beyond transfusion and iron chelation is emerging in the thalassemia realm to improve outcomes and

overall quality of life (Dreuzy *et al.*, 2019). In coming years, gene transfer and gene editing technology will probably confirm the treatment of thalassemia (Roselliet *al.*, 2010; Nienhuis *et al.*, 2012; Bouladet *al.*, 2014; Karponiet *al.*, 2019). Similar kind of studies have substantiated the findings of the present study (Pignatti *et al.*, 2011; Ansari *et al.*, 2014; Suriyany *et al.*, 2021; Aphidechkul, 2021). Anemia is primarily prevalent due to improper diet, workload, stress and physiological burden. Specifically, in adolescent girls, malnourished children and females with early age pregnancies usually suffer from anemia. Simultaneously, primary reasons for Haemoglobinopathies are education, insufficient degree of awareness, and congenital marriages, particularly in tribes and communities where congenial marriages are in practice.

Conclusion

The present study showed that the prevalence of anemia is very high in Kumaun Region. If proper measures would not be adopted, it will lead to other complications and become a significant public health concern in India. Nutritional deficiency anemia is the most common cause of Anemia among the population and iron deficiency is the most common nutritional deficiency in the population. Low socio-economic class, worm infestation and multiple pregnancies are the most common risk factor related to Anemia. Vegetarian diet, false dietary habits, Improving education and empowering them is also essential to make better dietary choices for themselves and their families. Similarly, hemoglobinopathies can be checked and addressed by using medical and social interventions in a targeted population.

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