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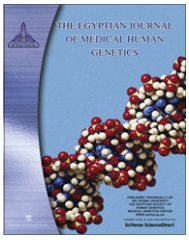

ORIGINAL ARTICLE

# Gene frequency of sickle cell trait among Muslim populations in a malarial belt of India, i.e., Manipur

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**KEYWORDS**

Sickle cell trait;
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Heterozygosity

**Abstract** *Background:* Sickle cell anaemia is an important genetic and public health problem in Manipur, which is a small hilly state, situated at the north eastern extreme corner of India sharing an international boundary with Myanmar. Our present study provides a comprehensive database on the occurrence of sickle cell trait in the Manipuri population especially with regard to Manipuri Muslims, as till date no work has been done on Manipuri Muslims with different castes.

*Aim:* To study the gene frequency and heterozygosity condition of sickle cell trait in different populations of Manipur.

*Subjects and methods:* We have undertaken a survey of the frequencies of sickle cell gene among Muslims with different castes, viz., Sheikh, Syed, Pathan and Moghul; Hindu (Meitei) and tribe (Naga). The blood samples were collected by finger-prick method and were tested for sickle cell trait by the wet sealed method using 2% freshly prepared sodium metabisulphite solution following the method of Daland and Castle.

*Results:* The Moghul population shows the highest allele frequency of sickle cell gene, i.e., 16.96% while Naga shows the least, i.e., 8.6%. Females show a higher allele frequency of the sickle cell gene, i.e., 29.83% than males who show a frequency of 21.99%. The heterozygosity condition was found to be higher among Mughals, i.e., 28.12% while the least is exhibited by Naga, i.e., 15.72%. Higher percentage of sickle cell trait in this region might be resulting from the natural selection process in response to the high prevalence of malaria (*Plasmodium falciparum*) in Manipur to protect the inhabitants from the lethal effects of malaria.



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## 1. Introduction

India is a store house of varied geographic landscape, consisting of 28 states to which are included the seven north eastern states popularly known as seven sisters. The north east is inhabited by a diverse population of tribes, castes, religious and migrant populations. The region is particularly interesting as represented by several tribal populations of mongoloid origin, who have migrated from eastern and south east Asian regions and settled in different parts during several waves of migration [1,2]. They share similar physical features but speak different languages and show differences in cultural, anthropological and genetical traits [3,4]. The topography of North East India, flanked in the north by the Himalayas and in the south by the Bay of Bengal, constitutes a unique narrow passage that connects the Indian subcontinent to East Asia and South East Asia through a 2000 km eastern border, shared with five neighbouring countries.

Manipur (Fig. 1), one of the states of this region, is a small hilly state, situated in the north eastern extreme corner of India that connects the Indian subcontinent to East Asia and South East Asia as a unique narrow passageway [5]. Manipur is situated between 23.83° north latitude to 25.68° north latitude and 93.03° east longitude to 94.78° east longitude. The territory of Manipur includes an area of 22,327 $km^2$ in which the hilly area (92% of the land) surrounds the centre of the valley area (8%) [6]. The hilly region occupies a large area of 20,571 $km^2$. It has a wonderful balance of the flora and fauna by a combination of wet forest and temperate forest. This state, however small, is an abode of a number of Mongoloid groups, who speak different dialects of the Tibeto-Burman linguistic family. There are also a few groups who possess Caucasoid and Australoid racial elements [7].

Malaria is a serious public health problem in Laos [8], which is a land-locked country bordering Thailand, Combodia, Myanmar, Vietnam and China. Malaria is also the most common infectious cause of morbidity and mortality in Vietnam as it is in many developing countries in the tropics [9]. These reports can confirm the importance and high prevalence of malaria in Thailand and nearby Indo-China countries which of course includes Manipur [10]. As natural selection works on the whole individual, heritable traits will become more common in the next generation. Given enough time, this passive process can result in progressive adaptation and speciation.

Sickle cell trait (SCT) occurs in approximately 300 million people worldwide, with high prevalence in Africa, the Arabian Peninsula, India, the Mediterranean, and the southern United States [11]. The trait is characterised by the inheritance of a normal haemoglobin gene (HbA) from one parent and an abnormal mutated beta globin gene, the sickle haemoglobin gene (HbS) from the other parent. In sickle cell disease, two abnormal allelomorphic haemoglobin genes are inherited, of which at least one must be the sickle haemoglobin. In the homozygous sickle cell disease (HbSS), both abnormal haemoglobins are HbS. Normal adult haemoglobin is made from a combination of two beta and two alpha globin chains and a haeme. The beta1-globin gene is located on the short arm of chromosome 11. Approximately 150 diseases have been linked to the same chromosome 11 [12]. The sickle gene is multicentric in origin, and four main haplotypes, representing four different mutations, have been identified [13].

The genetic change yields the red blood cells (RBC), to have a short life span of 10–20 days in comparison to the normal RBC life span of 120 days. Homozygote for this allele suffers from a severe form of anaemia in which haemoglobin crystallises in the blood, distorting the shape of the RBC. Sometimes the cells appear sickle shaped giving the disease the name Sickle cell anaemia. These sickle shaped cells also clog small blood vessels and cut off oxygen transport to various tissues. The heterozygous carriers of the mutant allele do not show disease symptoms unless they travel to high altitudes, where the oxygen concentration is low. These individuals, therefore, are said to possess the sickle cell trait [14]. Epidemiological studies have shown the wild type homozygotes to be more susceptible to infection by malarial parasites than heterozygotes. As a result, both kinds of homozygotes in this system are less fit than the heterozygotes.

The 20 million people of India are known to suffer from sickle cell disease [15]. The highest frequency of sickle cell gene in India is reported from Orissa, followed by Assam, Madhya Pradesh, Uttar Pradesh, Tamil Nadu and Gujarat [16]. The average frequency of sickle gene is 4.3%, while that in Orissa is 9.1% [17]. The population diversity of sickle cell haemoglobinopathy in India mainly is the result of the admixture of genes between different populations, e.g. intruders or invading groups in and around the Gulf region, from Middle Eastern countries and Africa [18–21]. Epidemiologically, children comprise 52% of sickle cell patients. The three predominant forms (SS, SB and SD) of the disease are clinically and haematologically indistinguishable [22]. The range of the disease varies from 0% to 44%. It is 0–18.5% in north east zone, 0–33.5% in the west zone, 22.5–44.4% in the central zone and 1–40% in the southern zone [23].

## 2. Subjects and methods

### 2.1. Populations

The Muslims of India comprise more than 13% of the population, and they belong to various castes, based on linguistic and ethnic groups besides, having a few tribes [24]. Manipuri Muslims comprise 8.32% of the total population, according to the 2001 census. They are mostly the migrants who started coming to the state in the middle of the 16th century [25]. They have been given different clan names which in Manipuri is called Yumnak or Sagei. The term ''Sagei'' is a corrupted word of Shaqzi which is an Urdu terminology.

About 74 clans are reported in Manipur in the present times. Manipuri Muslims belong to Sheikh, Syed, Pathan or Mughal castes [26], they belong to Sunni sect only. The Meiteis represent the major tribal group, having 60% of the total population [27] and they follow Hindu religion. Meiteis are presumably formed by the admixture of Koomal, Looang, Moirang and Meitei, all of whom are reported to have arrived at different periods of time, coming from different directions and now represent the clans of the community [25]. While the Naga are the indigenous tribal population of Manipur, they belong to the Naga–Kuki–Chin group of the Tibeto-Burman linguistic family and are believed to have migrated to Manipur from Burma probably 300–400 years ago [28].