International Journal of Current Research and Review
DOI: http://dx.doi.org/10.31782/IJCRR.2022.14201

Original Research

IJCRR
Section: Healthcare
ISI Impact Factor (2020-21): 1.899
IC Value (2020): 91.47
SJIF (2020) = 7.893

Geospatial Mapping of Genetic Diseases in the Southern Karnataka, India: A Novel Approach in Medical Technology

Mohandas Aparna[1]*, Kumar Sunil D[2], Bhat Deepa[3], Murthy Narayana MR[4], Gopi Arun[5]

[1]Final year Post Graduate, Department of Community Medicine, JSS Medical College, JSS Academy of Higher Education and Research, Sri Shivarathreeshwara Nagara, Mysuru-570015, Karnataka, India; [2]Associate Professor, Department of Community Medicine, JSS Medical College, JSS Academy of Higher Education and Research, Sri Shivarathreeshwara Nagara Mysuru-570015, Karnataka, India; [3]Associate Professor, Department of Anatomy, JSS Medical College, JSS Academy of Higher Education and Research, Sri Shivarathreeshwara Nagara Mysuru-570015, Karnataka, India; [4]Professor and Head of the Department, Department of Community Medicine, JSS Medical College, JSS Academy of Higher Education and Research, Sri Shivarathreeshwara Nagara Mysuru-570015, Karnataka, India; [5]Lecturer in statistics, Department of Community Medicine, JSS Medical College, JSS Academy of Higher Education and Research, Sri Shivarathreeshwara Nagara Mysuru-570015, Karnataka, India.

ABSTRACT

Introduction: India records almost all known genetic disease, however surveillance activities and services are limited. Geographical information system (GIS) can act as a useful tool for surveillance.

Aims: The aim of the study was to assess the geospatial distribution of genetic diseases in Southern Karnataka, India and to describe their clinico-epidemiological profile.

Methodology: A cross-sectional study was conducted among 101 genetic disease patients attending the Genetic clinic of a tertiary care hospital. Data regarding the socio-demographic and clinico-epidemiological profile of the patients were collected using a semi-structured questionnaire. The geographical co-ordinates of the patients' addresses were recorded. Statistical analysis was performed using SPSS Version 22 and QGIS software Version 3.16.3 "Hannover" was used to create the maps. Qualitative variables were represented using proportions. Association between qualitative variables were inferred using Chi-square test.

Results: Geospatial mapping showed that functional genetic diseases were more compared to structural genetic diseases. Among the 101 patients, 66(65.34%) were males, 34(33.66%) were females and 1(0.99%) belonged to the other gender. 17.82% were born of a 2nd degree and 25.74% from a 3rd degree consanguineous marriage. 3(2.97%) of mothers were above the age of 35 years. 75(74.25%) had gene defects, 13(12.87%) had chromosomal diseases, 7(6.93%) had mitochondrial diseases and 6(5.94%) had multifactorial diseases.

Conclusion: It is evident from the geospatial mapping that both structural and functional genetic diseases have a widespread distribution in the population and is no longer a "rare disease". It is the need of the hour to expand surveillance activities.

Key Words: Congenital anomaly, Genetic diseases, Geographical information system, Geospatial mapping, Rare diseases, Surveillance

INTRODUCTION

Annually, 7.9 million children suffer from a grave congenital anomaly of genetic etiology which contributes to 3.3 million deaths. The major contributors of genetic diseases being a family history of such diseases, carrier state in the parents, consanguineous marriage, advanced maternal age, and maternal exposure to teratogenic drugs, radiations or chemicals, infections like syphilis, rubella and use of recreational drugs, tobacco and alcohol.[1] Chromosomal disorders add to 6% of birth defects, Down syndrome being the most common of them.[1,2] The next major group are the single gene defects which accounts for 1 in 1000 live births, the two most predominant diseases being Sickle cell anemia and Thalassemia.[3,4] It is estimated that about 5% of the global population carries trait for hemoglobin disorders and 3 to 5 lakh children who are delivered annually suffer from them.[4,5]

Corresponding Author:
Mohandas Aparna, Final year Post Graduate, Department of Community Medicine, JSS Medical College, JSS Academy of Higher Education and Research, Sri Shivarathreeshwara Nagara Mysuru-570015, Karnataka, India; Contact: 495609519; Email: aparnacnair90@gmail.com

ISSN: 2231-2196 (Print) **ISSN:** 0975-5241 (Online)

Received: 26.05.2021 **Revised:** 12.07.2021 **Accepted:** 04.09.2021 **Published:** 16.01.2022

India as such has a high burden of Down syndrome, inborn errors of metabolism and hemoglobin disorders like Sickle cell anemia and Thalassemia.[6] In India, Down syndrome affects 1 in every 900 children.[7] As far as hemoglobin disorders are concerned, at one point of time there are about 1.5 lakh cases of Sickle cell anemia and 1 lakh cases of beta Thalassemia. It is more predominant amongst the scheduled subpopulation of the country, the prevalence of Thalassemia ranging between 4-17% amongst them.[4] Another important group are the inborn errors of metabolism and in India, 5-15% of newborns, yearly, suffer from these. Newborn screening is a simple method of identifying the affected children to initiate early treatment and to prevent disabilities and also to offer prenatal diagnosis in the future pregnancies, however the services offered in India are limited.[8]

Over the years, the burden of genetic diseases has increased, also the advancement in various dimensions has increased survival, adding on to the morbidity and impairment due to genetic diseases. While some countries, like in the United Kingdom have already incorporated neonatal and antenatal screening for hereditary diseases in their health system, the economically backward countries which contribute to nearly 94% of the infants with genetic defects, lack in public health policies for care and prevention of genetic diseases.[9] Reducing the burden of genetic diseases should begin with active and passive surveillance in the community and at the hospital setting with partnership of laboratories and research institutes. This shall help to lay the foundation by assessing the burden and trends in various geographic locations across the country. It is high time that genetic screening and counselling be incorporated into the existing health care delivery system. Expansion of diagnostics with adequate treatment and rehabilitative services also becomes a prerequisite.[10,11]

Geographical information system (GIS) is a tool that combines spatial information with attributable data and assembles them as layers. GIS helps to build up these layers into visualizations using maps, which reveal patterns and relationships between spatial data and attribute data.[12] With regard to genetic diseases, GIS can be used to investigate the spatial form of distribution of these diseases and the associated spatial determinants which can play an important role in estimating the prevalence of genetic diseases across the country and also to assess the gaps in the existing service delivery system.[13]

With this background, the present study was conducted to assess the geospatial distribution of genetic diseases in Southern Karnataka, India and to describe their clinico-epidemiological profile.

MATERIALS AND METHODS

Study design and population

This cross-sectional study was conducted for one and half years from January 2019 to July 2020 among patients attending the genetic clinic of a tertiary care hospital, Southern Karnataka, India. Consecutive sampling was used to select the participants. Participants with genetic diseases who were willing to participate in the study were included and those who were not confirmed as genetic diseases by laboratory diagnosis were excluded from the study.

Ethical statement

The study was commenced after presenting the protocol and obtaining ethical clearance from the institutional ethics committee. IEC NO: JSS/MC/PG/4623/2018-19

Before beginning the collection of data, the study details were explained to the patients or parents as relevant. Verbal assent was taken from children below 18 years and written informed consent was taken from parents/patients as appropriate.

Data collection

Data was collected by interview method using a semi-structured questionnaire regarding the sociodemographic factors (age, gender, religion, address, occupation, type of family) and regarding family history, previous obstetric history and antenatal history. Relevant birth history, clinical and investigation history and diagnosis of the patient was recorded.

Final diagnosis of the patient was obtained and categorized as structural or functional genetic diseases.

Structural diseases- Refers to defects in body structure including skeletal system and organs. It includes external as well as internal defects. Includes neural tube defects, cleft lip, cleft palate, congenital heart diseases, Down syndrome, Edward syndrome, cystic kidney disease, skeletal and limb deformities and indeterminate sex.

Functional diseases- Functional defects in the neurological, muscular immunological or endocrine system. Includes metabolic disorders, cystic fibrosis, muscular dystrophy, behavioral disorders and neurological disorders.[14]

Statistical analysis

Data was entered into Microsoft Excel 2013 spreadsheet and analyzed using SPSS V.22 (Licensed to JSS AHER). Qualitative variables like gender, religion, place of residence, etc. were represented using proportions. Association between qualitative variables were inferred using Chi-square test. A p value less than 0.05 was considered statistically significant.

Geospatial analysis

Freely accessible online sources were used to geocode the address of the study participants. The latitude and longitude were entered in Microsoft Excel and converted into CSV file (comma separated values) and exported into a free and open-source software version QGIS 3.16.3 "Hannover" (released on 15.01.2021) to create maps.

RESULTS

Figure 1, depicts the map of southern Karnataka, India and the distribution of the study participants based on gender. The majority were males in the present study. Among the 101 study participants, majority of the parents gave a history of non-consanguineous marriage (**Figure 2**). **Figure 3**, gives the classification of study participants based on the type of genetic diseases. In the study, functional genetic diseases were more, compared to structural genetic diseases.

Among the 101 study participants, 10(9.9%) were below 6 months, 40(39.60%) were between the age of 6 months to 1 year, 21(20.79%) between 1 to 5 years, 13(12.87%) were between 5 to 10 years and 17(16.83%) were above the age of 10 years. 3(2.97%) of the mothers were above the age of 35 years at the time of conception. Among the 101 genetic disease patients, 56.43% were born of a non-consanguineous marriage, while 18.81% and 24.75% were born of a 2nd and 3rd degree consanguineous marriage, respectively. Among the mothers, 27.72% gave a history of previous abortions/ neonatal death/stillbirths while 72.27% did not have such history. 2(1.98%) of the mothers gave history of fever during pregnancy. 73(72.27%) of the participants were of normal birth weight while 28(27.73%) had low birth weight. 89.10% of the study participants were term babies and 10.89% were preterm babies. In 11.88% of the cases, sibling had similar disease. In the 101 study participants, 65(64.35%) had functional genetic diseases and 36(35.64%) had structural genetic diseases (**Table 1**).

On classification of genetic diseases, 75(74.25%) had gene defects, 13(12.87%) had chromosomal diseases, of which Down syndrome (9.9%) was the majority, 7(6.93%) had mitochondrial diseases and 6(5.94%) had multifactorial diseases (**Table 2**).

Table 3, represents the association between socio-demographic and clinico-epidemiological factors with genetic diseases. There was a significant association between gender and socio-economic class with genetic diseases. 3 (2.97%) of the mothers were above the age of 35 years and all of them had children with structural anomalies. There was a significant association between maternal age at conception and paternal medical conditions with genetic diseases in the children. 3(2.97%) of fathers had Diabetes Mellitus and they had children with structural anomalies.

DISCUSSION

Geocoding is an important GIS tool used in public health for surveillance activities.[15] Disease surveillance tracks data related to incidence/ prevalence of the disease, its spread and possible risk factors which shall give the pattern and trend of the disease.[16] In the present study, locations of the patients were mapped. Functional genetic diseases accounted for the majority compared to structural genetic diseases. It is evident from the visualization that genetic diseases are not 'rare' as thought to be earlier, but rather have a widespread distribution across the population. GIS has an important role in scenarios wherein it can be utilized to study the distribution of genetic diseases, associated gene mutations and their trend over the years. This shall help to identify cluster areas as well develop causal relationships.[17]In our study we have considered all genetic diseases, and it would require disease specific genetic studies to make such conclusions.

Among 101 study participants, 65.34% were males, 33.66% were females and 1(0.99%) belonged to other gender. Similar findings were reported by Lavanya et al. and Jayasree et al.. in institutional based studies in south India. It is suggested that females are affected more with lethal defects and cannot survive till term gestation.[18,19] Genetic diseases were more among the lower socioeconomic class in our study. This can be attributed to the predominance of consanguineous marriage and poor maternal health, added with higher exposure to environmental risk factors among them.[1,20]

In the present study 97.02% of the mothers were below the age of 35 years at conception. Majority of the studies suggest the same, bulk of genetic diseases are reported among mothers less than 35 years, owing to the fact that in India, major proportion of deliveries take place before the mother reaches 35 years.[18,19] However among the 3% mothers above the age of 35 years, all had children with structural anomalies. This is consistent with the findings that advanced maternal age is associated with higher risk of chromosomal abnormalities.[1] Among 101 study participants, majority were born out of non-consanguineous marriage. Structural and functional genetic disease proportion were similar in non-consanguineous and consanguineous marriage. Jayasree et al. reported that only 1% of children with congenital anomalies were born out of a consanguineous marriage.[19] Rama devi et al. suggests that in the background of various other environmental factors contributing to the burden of genetic diseases, the role of consanguinity may have been masked.[20] 27.72% of the mothers in our study gave a history of previous abortion/neonatal deaths and stillbirths. Jayasree et al. in a study in Kerala reported that 25.1% of the women who gave birth to a child with congenital anomaly had previous history of abortions or intrauterine deaths (IUD) or neonatal deaths.[19] This can be due to the fact that many genetic diseases are lethal and

cause fetal death and hence women with a bad obstetric history are at higher risk.[21]

In our study, 2.97% of fathers had Diabetes Mellitus and all of these children had structural genetic diseases. However, Mills et al. reported that children born to diabetic fathers had the same risk of developing malformations compared to non-diabetic fathers.[22] 11.88% of the cases had similar conditions in the sibling. El Kowmi et al. reported that 6% of the affected children in their study had a history of an anomaly in the family, signifying that genetic diseases tend to recur and requires evaluation so as to prevent the same conditions in future pregnancies.[23]

In the present study, 12.87% had chromosomal abnormalities, 74.25% had single gene defects, 6.93% had mitochondrial diseases and 5.94% had multifactorial diseases. Rama devi et al. in a study in Karnataka reported the prevalence of single-gene disorders to be higher followed by multifactorial disorders.[20] The most common chromosomal abnormality in our study was Down syndrome (9.9%). Similar findings were reported by Kaur et al., where the prevalence was 11% and Wojnik et al. who reported a prevalence of 30% among chromosomal disorders.[24,25]

Among the single gene disorders, most common were the inborn errors of metabolism-organic acidemia's (12.87%) and Lysosomal storage disorders (8.91%). Similar findings were quoted by Verma et al. from a multi-center study where the prevalence of organic acidurias were maximum (27.5%).[21] The proportion of Duchenne muscular dystrophy was 5.94% and other common dystrophy was Limb girdle musculodystrophy (1.98%) in this study. 2.97% had spinal muscular atrophy. Kaur et al. reported an overall proportion of muscular dystrophies to be 0.8% and Wojnik et al. reported the prevalence of spinal muscular atrophies to be 16% which is quite higher compared to our study, probably because of the difference in size of the sample and study setting.[24,25] 1.98% of study participants had sickle cell anemia and Thalassemia in this study. The prevalence of Beta-Thalassemia trait being 3-4% and Sickle cell anemia allele being 2-20% in India.[6] 5.94% had multifactorial diseases in our study. Verma et al. quotes a prevalence of 4.64%. The most common ones being cleft lip/cleft palate and multiple anomalies.[21] Kaur et al. reported a proportion of 0.1% in her study while Rama devi et al. reported 2 in 12 cases of polygenic inheritance for cleft lip/cleft palate.[20,24]

Limitations

Since this was a hospital based study, the address provided by the patients were used for geocoding their locations and we could not confirm the accuracy of it. The sample was limited, hence we have given proportions for the various parameters assessed. It would require a community based study to assess the prevalence of genetic diseases.

CONCLUSION

It is evident from the geospatial mapping that both structural and functional genetic diseases have a widespread distribution in the population and is no longer a "rare disease" as described earlier. Genetic diseases being a rising cause of childhood morbidity and mortality in India, it is the need of the hour to expand surveillance activities, incorporate newborn screening into the routine biochemical testing and to provide adequate diagnostic services to the suspected with preventive services like carrier screening and counselling.

ACKNOWLEDGEMENT

We thank the study participants and their families for their time and co-operation.

Financial support: None

Conflict of interest: None

Author's contribution

Mohandas Aparna: Conceptualization, Methodology, Formal analysis, Investigation, Data curation, Writing-original draft, writing-review and editing. **Kumar Sunil D:** Conceptualization, Methodology, Supervision, Data curation, writing-review and editing. **Bhat Deepa:** Conceptualization, Methodology, Investigation, writing-review and editing. **Murthy Narayana M.R:** Methodology, Supervision, Data curation, writing-review and editing. **Gopi Arun:** Methodology, Data curation, Formal analysis, writing-review and editing.

REFERENCES

1. Christianson A, Howson CP, Modell B. March of Dimes: global report on birth defects, the hidden toll of dying and disabled children. New York: March of Dimes Birth Defects Foundation; 2006.84p.
2. Bhavani V, Paulose D. Spinal Anaesthesia in Down's syndrome-A Case Report. Int J Cur Res Rev 2015 May;7(9):33.
3. National Human Genome Research Institute. Genetic Disorders [Internet]. Bethesda: National Human Genome Research Institute; [updated 2018 May 18; cited 2020 Sep 30]. Available from: https://www.genome.gov/For-Patients-and-Families/Genetic-Disorders
4. Colah R, Italia K, Gorakshakar A. Burden of thalassemia in India: The road map for control. Pediatr Hematol Oncol J 2017 Dec;2(4):79–84.
5. Kadri AM. Genetics and health. In: Kundapur R, Maroof A.K, editors. IAPSM's Textbook of Community Medicine. 1st ed. Haryana: Jaypee Brothers Medical Publishers (P) Ltd; 2019. p. 836-839.
6. GUaRDIAN Consortium, Sivasubbu S, Scaria V. Genomics of rare genetic diseases—experiences from India. Hum Genomics 2019 Dec;13(1):1-8.
7. Pankaj G, Avani K, Salil V. Prevalence of Down syndrome in Western India: A Cytogenetic Study. Br J Med Med Res 2015 Jan;5(10):1255–1259.

8. Kapoor S, Thelma BK. Status of Newborn Screening and Inborn Errors of Metabolism in India. Indian J Pediatr 2018 Dec;85(12):1110–1117.
9. World Health Organization. Congenital anomalies [Internet]. Geneva: World Health Organization; [updated 2020 Dec 1; cited 2020 Sep 30]. Available from: https://www.who.int/news-room/fact-sheets/detail/congenital-anomalies
10. Burton H, Jackson C, Abubakar I. The impact of genomics on public health practice. Brit Med Bull 2014 Dec;112(1):37–46.
11. Wang G, Watts C. The Role of Genetics in the Provision of Essential Public Health Services. Am J Public Health 2007 Apr;97(4):620–625.
12. Environmental Systems Research Institute. What is GIS? [Internet]. California: Environmental Systems Research Institute; [cited 2020 Nov 19]. Available from: https://www.esri.com/en-us/what-is-gis/overview
13. Ananth M, Rajesh R, Amjith R, AL A, Valamparampil MJ, Harikrishnan M, et al.. Contamination of household open wells in an urban area of Trivandrum, Kerala State, India: a spatial analysis of health risk using geographic information system. Environ Health Insights 2018;1-9.
14. Birth Defect Research for Children. Structural and Functional Birth Defects [Internet]. Florida: Birth Defect Research for Children; 2020[cited 2020 Oct 27]. Available from: https://birthdefects.org/structural-and-functional-birth-defects/
15. Chang KT. Geocoding and Dynamic Segmentation. Introduction to geographic information systems. 9th ed. New York: McGraw-Hill Education; 2018.p.363-364.
16. Shaw N.T, McGuire S.K. Understanding the use of geographical information systems (GISs) in health informatics research: a review. J Innov Health Inform 2017 Jun;24(2):228–233.
17. Hockham C, Bhatt S, Colah R, Mukherjee MB, Penman BS, Gupta S, et al.. The spatial epidemiology of sickle-cell anaemia in India. Sci Rep 2018 Dec;8(1):1-10.
18. Lavanya S, Seethalakshmi V. A two-year study of patterns and prevalence of congenital malformations. Int J Reprod Contracept Obstet Gynecol 2018;7(1):114-118.
19. S. Jayasree, D'Couth S. Prevalence of congenital anomalies in a tertiary care centre in North Kerala, India. Int J Reprod Contracept Obstet Gynecol 2018 Mar;7(3):864-869.
20. Devi AR, Rao NA, Bittles AH. Inbreeding and the incidence of childhood genetic disorders in Karnataka, South India. J Med Genet 1987 Jun;24(6):362–365.
21. Verma IC, Puri RD. Global burden of genetic disease and the role of genetic screening. Semin Fetal Neonatal Med 2015 Oct;20(5):354-363
22. Mills JL. Malformations in infants of diabetic mothers. Birth Defects Res A Clin Mol Teratol 2010 Oct;88(10):769–778.
23. El Koumi MA, Al Banna EA, Lebda I. Pattern of congenital anomalies in newborn: a hospital-based study. Pediatr Rep 2013 Feb;5(1):20-23.
24. Kaur A, Singh JR. Chromosomal Abnormalities: Genetic Disease Burden in India. Int J Hum Genet 2010 Mar;10(1 Suppl 3):1–14.
25. Wojcik MH, Schwartz TS, Thiele KE, Paterson H, Stadelmaier R, Mullen TE, et al.. Infant mortality: the contribution of genetic disorders. J Perinatol 2019 Dec;39(12):1611–1619.

Table 1: Socio-demographic and clinico-epidemiological profile of the genetic disease patients; N=101

Variables		Total
Gender	Male	66(65.34%)
	Female	34(33.66%)
	Other gender	1(0.99%)
Place of residence	Urban	48(47.52%)
	Rural	53(52.47%)
Religion	Hindu	84(83.16%)
	Muslim	16(15.84%)
	Christian	1(0.99%)
Socio-economic class (B.G Prasad classification	Upper class	9(8.91%)
	Upper middle class	17(16.83%)
	Middle class	11(10.89%)
	Lower middle class	29(28.71%)
	Lower class	35(34.65%)
Paternal	<40 years	96(95.04%)
age	>/= 40 years	5(4.95%)
Maternal age	<35 years	98(97.02%)
	>/= 35 years	3(2.97%)
Type of marriage of parents	Non-consanguineous	57(56.43%)
	Consanguineous	44(43.57%)

Table 1: ***(Continued)***

Variables		Total
Maternal medical history	No	89(88.11%)
	GDM	2(1.98%)
	Pregnancy induced hypertension	2(1.98%)
	GDM with PIH	1(0.99%)
	Hypothyroidism	4(3.96%)
	Pancreatitis	2(1.98%)
	ADPKD	1(0.99%)
Paternal medical history	No	96(95.04%)
	Diabetes Mellitus	3(2.97%)
	Depression	1(0.99%)
	Hyperthyroidism	1(0.99%)

Table 2: Classification of genetic diseases in the study participants; N=101

Disease			Frequency	Percentage
	Chromosomal abnormalities	Down syndrome	10	9.9%
		Edward Syndrome	1	0.99%
		Partial trisomy 15	1	0.99%
		DiGeorge syndrome	1	0.99%
	Total		13	12.87%
	Single gene disorders	Neurofibromatosis Type 2	1	0.99%
		Autosomal dominant polycystic kidney disease	1	0.99%
		Cystic fibrosis	3	2.97%
		Limb girdle musculodystrophy	2	1.98%
		Spinal muscular atrophy	3	2.97%
		Duchenne muscular dystrophy	6	5.94%
		Sickle cell anemia	2	1.98%
		Thalassemia	2	1.98%
		Achondroplasia	1	0.99%
		Noonan's syndrome	1	0.99%
		Alport's syndrome	1	0.99%
		Tuberous sclerosis	2	1.98%
		Hereditary sensorineural hearing loss	2	1.98%
		Jervell and Lange-Nielson syndrome	1	0.99%
		Fragile X	2	1.98%
		Cornelia de Lange syndrome	1	0.99%
		Metachromatic adult leucodystrophy	1	0.99%
		Apert syndrome	1	0.99%
		Russell-Silver syndrome	3	2.97%
		Osteogenesis imperfecta	3	2.97%
		Cerebellar ataxia	1	0.99%
	Metabolic disorders	Gilbert syndrome	1	0.99%
		Hereditary pancreatitis	1	0.99%

Table 2: ***(Continued)***

Disease			Frequency	Percentage
		Hereditary hypoglycemia	1	0.99%
		Haemochromatosis	1	0.99%
		Surfactant deficiency	1	0.99%
		G6PD deficiency	3	2.97%
	Aminoacidopathies	Phenyl ketonuria	1	0.99%
		Cystinosis	2	1.98%
		Tyrosenemia	1	0.99%
	Organic acidemia's		13	12.87%
	Lysosomal storage disorders	Gauchers disease	3	2.97%
		Niemann-Pick disease	2	1.98%
		Mucopolysaccharidosis	4	3.96%
	Urea cycle defect	Citrullinemia	1	0.99%
	Total		75	74.25%
	Mitochondrial diseases		7	6.93%
	Total		7	6.93%
	Multifactorial diseases	Cleft lip/cleft palate	2	1.98%
		Ambiguous genitalia	1	0.99%
		Multiple congenital defects	3	2.97%
	Total		6	5.94%

Table 3: Association between socio-demographic and clinic-epidemiological factors and genetic diseases; N=101

Variables		Structural genetic diseases	Functional genetic diseases	Total	Chi-square value	p value
Gender	Male	19 (28.8%)	47 (71.2%)	66 (100%)	4.946	**.046***
	Female	16 (47.1%)	18 (52.9%)	34 (100%)		
	Other gender	1 (100%)	0	1 (100%)		
Religion	Hindu	30 (35.7%)	54 (64.3%)	84 (100%)	1.810	.522
	Muslim	5 (31.3%)	11 (68.8%)	16 (100%)		
	Christian	1 (100%)	0	1 (100%)		
Socio-economic class(B.G Prasad classification	Upper class	3 (33.3%)	6 (66.7%)	9 (100%)	9.797	**.039***
	Upper middle class	1 (5.9%)	16 (94.1%)	17 (100%)		
	Middle class	4 (36.4%)	7 (63.6%)	11 (100%)		
	Lower middle class	14 (48.3%)	15 (51.7%)	29 (100%)		
	Lower class	14 (40%)	21 (60%)	35 (100%)		

Table 3: ***(Continued)***

Variables		Structural genetic diseases	Functional genetic diseases	Total	Chi-square value	p value
Paternal age	<40 years	33 (34.4%)	63 (65.6%)	96 (100%)	1.290	.241
	>/= 40 years	3 (60%)	2 (40%)	5 (100%)		
Maternal age	<35 years	33 (33.7%)	65 (66.3%)	98 (100%)	6.357	**.043***
	>/= 35 years	3 (100%)	0	3 (100%)		
Type of marriage of parents	Non-consanguineous	22 (38.6%)	35 (61.4%)	57 (100%)	.500	.534
	Consanguineous	14 (31.8%)	30 (68.2%)	44 (100%)		
Maternal medical history	No	32 (36%)	57 (64%)	89 (100%)	3.755	.877
	Diabetes Mellitus	1 (50%)	1 (50%)	2 (100%)		
	Pregnancy induced hypertension	1 (33.3%)	2 (66.7%)	3 (100%)		
	GDM with PIH	1 (100%)	0	1 (100%)		
	Hypothyroidism	1 (33.3%)	2 (66.7%)	3 (100%)		
	Pancreatitis	0	2 (100%)	2 (100%)		
	ADPKD	1 (100%)	0	1 (100%)		
Paternal medical history	No	33 (34.4%)	63 (65.6%)	96 (100%)	5.809	**.043***
	Diabetes Mellitus	3 (100%)	0	3 (100%)		
	Depression	0	1 (100%)	1 (100%)		
	Hyperthyroidism	0	1 (100%)	1 (100%)		
Gestational age at birth	Term	31 (34.4%)	59 (65.6%)	90 (100%)	.503	.515
	Pre-term	5 (45.5%)	6 (54.5%)	11 (100%)		

** p- Value < 0.05 is statistically significant*

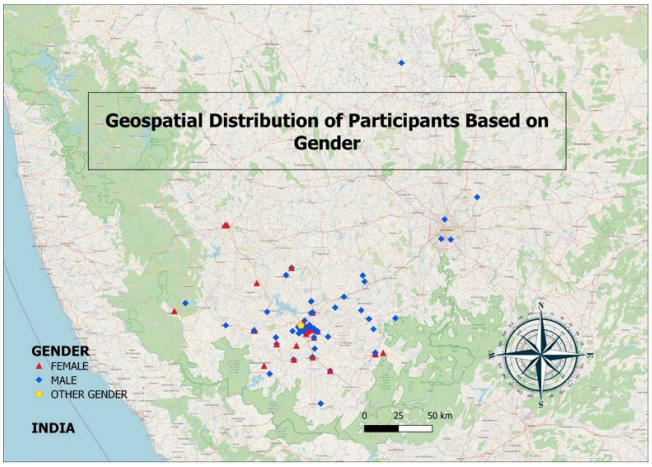

Figure 1: GIS map showing distribution of study participants based on gender.

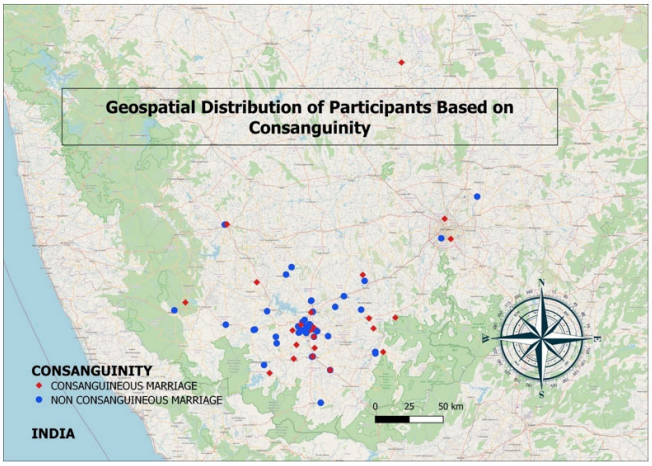

Figure 2: GIS map showing distribution of study participants based on the type of marriage of parents.

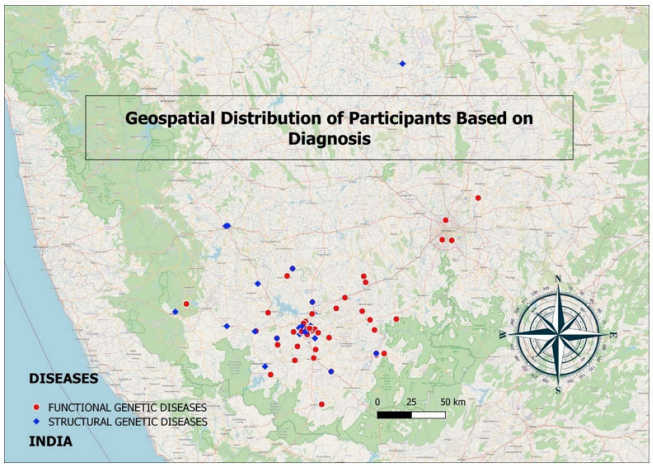

Figure 3: GIS map showing distribution of study participants based on the type of genetic disease.