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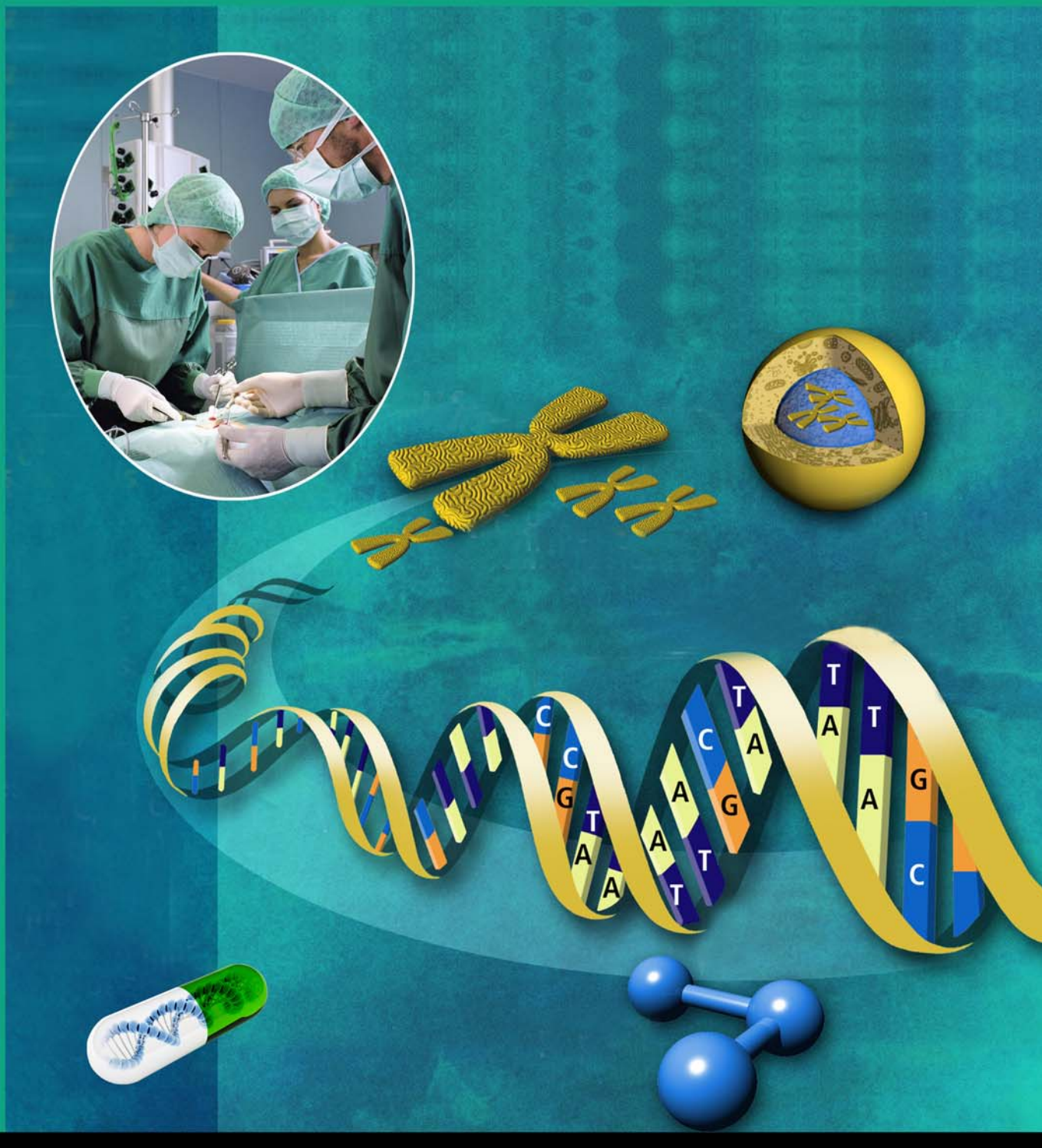

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Research Paper

A SURVEY ON THE PREVALENCE OF VITILIGO IN BANGALORE CITY, INDIA

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Vitiligo is a skin disorder that has been known for at least 5000 years, but it is still incompletely understood. It is considered to be a multifactorial polygenic disorder with a complex pathogenesis, linked with both genetic and non-genetic factors. It has baffled the medical world for centuries. It is a psychologically devastating clinical conundrum which affects all types of human races without any specificity and its incidences of occurrence have been rising alarmingly. Vitiligo is generally associated with a high psychiatric morbidity. The worldwide population prevalence of vitiligo ranges from 1% to 4% and shows a wide variability among ethnic groups. In India, the incidence of vitiligo has been reported to be between 1-2%. This paper reports the survey on the prevalence of vitiligo in Bangalore (India). The prevalence was found to be Vitiligo is 0.71%. A total of 22037 people were contacted in the survey cutting across all segments of the society. A total of 160 people were found to be affected in the survey. Out of the total 160 people affected, 65 are males (0.29%) while 95 were females (0.43%). The age specific prevalence was 0.15% for people below the age of 20, 0.24% for the age group between 20 to 30 years, 0. 18% for the age between 30 and 40 and was found to be 0.42% in people above 40 years. There was a significant difference with respect to the prevalence in people with different skin complexions, but there was no difference noticed among people of different socioeconomic groups. The people affected by vitiligo are called vitiligans (new term used first time) in this paper.

Keywords: Vitiligo, Leukoderma, Survey, Vitiligans

INTRODUCTION

Vitiligo is a skin disorder that has been known about for at least 5000 years, but not much has been done to understand its causes or to evaluate possible treatment. It is not a painful condition and perhaps that is why it is often trivialized and left untreated. The people affected by vitiligo are called *vitiligans* (new term used first time) in this paper. It is an acquired depigmentation disorder of great concern affecting 1-4% of the world population (Prasad *et al.,* 2003), still represents a cause of stigmatization and quality of life impairment in a large population. Vitiligo is by and large considered to be a multifactorial polygenic disorder with a complex pathogenesis, linked with both genetic and non-genetic factors. The precise

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process of manifestation and pathogenesis of this disorder still remains elusive. The disorder is now differentiated from the more inclusive and descriptive term leukoderma, which may also include depigmentations due to obvious local causes, such as burns or wounds, chronic eczematous conditions, psoriasis, leprosy, or syphilitic leukomelanoderma.

Vitiligo is medically known as *achromia* and is characterized by acquired, progressive, and circumscribed a melanosis of the skin and hair. Loss of cutaneous pigment appears to render the skin susceptible to premature aging and cancer. These susceptible and fragile melanocytes may undergo apoptosis. Autoimmune factors then perpetuate the removal of the melanocyte component from the skin. There is evidence to indicate that the pathophysiology of all forms of vitiligo are likely to involve autoimmune or inflammatory mechanisms. It is considered to be the most common hypopigmentary disorder, and is an acquired disease characterized by progressive loss of melanocytes. In almost half of patients, vitiligo starts before the age of 20 year, and males and females are affected with approximately equal frequency. Vitiligo itself has been classified based on clinical grounds into two major forms, namely, Segmental Vitiligo (SV) and Non-Segmental Vitiligo (NSV), the latter including several variants (Taïeb and Picardo, 2007 and 2009). A detailed classification is given in the Table 1. In 2011 Vitiligo European Taskforce (VETF) convened a consensus conference on issues of global importance for vitiligo clinical research. A consensus emerged that segmental vitiligo be classified separately from all other forms of vitiligo and that the term 'vitiligo' be used as an umbrella term for all non-segmental forms of vitiligo, including 'mixed vitiligo' in which segmental and non-segmental vitiligo are combined and which is considered a subgroup of vitiligo (Ezzedine *et al.*, 2011). There are several theories regarding the origin of vitiligo and loss of melanocytes and are based on autoimmunity, altered immunology, cytotoxicity, oxidant-antioxidant reactions, neurology, reactive oxygen species, contact and occupational mechanisms. The chances of oxidative stress-autoimmunity-

Table 1: Classification of vitiligo largely based on the discussions held during the Vitiligo Global Issue Consensus Conference held in 2011. Number of *vitiligans* found in the survey grouped in to different categories (it requires clearer definition)

Type of Vitiligo	Subtypes	Remarks
Non-segmental (NSV)	Focal, mucosal, acrofacial,	Sub-typing may not reflect a distinct nature, but useful information for epidemiologic studies
Segmental (SV)	Focal, mucosal, uni, bi or multi-segmental	Further classification according to distribution pattern possible.
Mixed (NSV+SV)	According to severity of SV	Usually the SV part in mixed vitiligo is more severe
Universal	Complete, nearly complete	It corresponds to complete or nearly complete depigmentation of the skin
Occupational/contact vitiligo	Based on the type of exposure	Acquired during job/work or by contacting fire or chemicals. Requires clearer definition
Undetermined/Unclassified	Uni-, bi-, or pluri-segmental	This category is a meant to allow, after a sufficient observation time (and if necessary investigations), to make a definitive classification

Table 2: Questionnaire Used in the Survey

S. No.	Sex: M/F	Age	Do you know about vitiligo?	Are you suffering from vitiligo?	If yes,			
					From when are you suffering	Which part is affected?	What medicines are you using?	Does anyone else in the family has it?
1	M	21	YES	NO				
2	M	20	YES	NO				
3	F	21	NO	NO				
4	M	19	YES	NO				

mediated melanocyte loss is also thought to be the reason for the appearance of this disorder. In spite of several theories, the pathogenesis of this disorder is still an enigma, but it appears to be dependent on the interaction of genetic, immunological, and neurological factors. Zinc-α2-glycoprotein (ZAG), a adipokine glycoprotein, secreted by a variety of normal epithelia is assigned to the chromosome 7q22.1. Bagherani (2012) has pointed that there is an association between vitiligo and ZAG. It is a multidisciplinary protein, which is secreted in various body fluids. ZAG is known to play roles in lipolysis, regulation of metabolism, cell proliferation and differentiation, regulation of melanin synthesis, cell adhesion, and immunoregulation. There is speculation on the interplay, if any, between Reactive Oxygen Species (ROS) and the immune system in the pathogenesis of vitiligo. There are scientific evidences linking oxidative stress and immune system to vitiligo pathogenesis giving credence to a convergent terminal pathway of oxidative stress-autoimmunity-mediated melanocyte loss (Laddha *et al.*, 2013). This indicates that immune system mis-identifies own pigment cells as 'foreign' and starts attacking them. Mosenson *et al.* (2013) have figured out that it is primarily a specific immune cell, the T cell, that is responsible for killing pigment cells, leaving the skin without a source of pigment. Depigmentation in vitiligans is found to be accompanied by accumulation of autoreactive CD8+ T cells in the skin, quantifiable loss of tyrosinase transcript, and local IFN-γ production. Neutralization of IFN-γ with antibody prevents CD8+ T cell accumulation and depigmentation. This was studied using a mouse model with focused epidermal depigmentation (Harris *et al.,* 2012). Linkage and genome-wide association studies identified 17 susceptibility loci for generalized vitiligo in the first phase of the study. In the second genome-wide association study, meta-analysis, and independent replication study, the same group has identified 13 additional vitiligo-associated loci, including OCA2- HERC2, a region of 16q24.3 containing MC1R, a region of chromosome 11q21 near TYR, several immunoregulatory loci including IFIH1, CD80, CLNK, BACH2, SLA, CASP7, CD44, IKZF4, SH2B3, and a region of 22q13.2. However the causal gene still remains uncertain (Jin *et al.*, 2012). Functional pathway analysis shows that most vitiligo susceptibility loci encode immunoregulatory proteins or melanocyte components that likely mediate immune targeting and genetic relationships among vitiligo, malignant melanoma, and normal variation of eye, skin, and

hair color. There have been major attempts to identify hereditary factors in vitiligo, and the genes identified to date support findings of Caroline Poole (contacted through e-mail, 2013) and her associates to support the fact that vitiligo is an autoimmune disease.

SURVEYS ON PREVALENCE AND INCIDENCE

There have been a very few reports of surveys conducted to study the prevalence and incidence of vitiligo worldwide. Such studies are scanty in India also. The population prevalence of vitiligo ranges from 0.1% to 2% and shows a wide variability among ethnic groups (Bolognia *et al*., 1998; Hann and Nordlund, 2000). For Caucasians in the United States and Northern Europe the estimated population prevalence of vitiligo is approximately 0.38% (Howitz *et al.*, 1977). Survey on the prevalence of vitiligo in the Isle of Bornholm, Denmark was carried out by Howitz *et al*. The prevalence of vitiligo was 0.38% in 47,033 people in a representative region in Denmark. Both sexes were equally affected. No significant difference was found in the distribution of 179 patients with vitiligo among five municipalities or between urban and rural districts. The age-specific prevalence increased from 0.09% under the age of 10 years to 0.90% in the age group 60 to 69 years. After the age of 70, the prevalence declined. This fall might reflect an increased incidence of vitiligo during the past few decades. The number of new cases of vitiligo increased steadily with advancing age, its onset being most often between the ages of 40 and 60 years. It is assumed that the prevalence of vitiligo in Denmark applies also to the northwestern part of Europe. A study was carried out in Calcutta, India by Das *et al.* (1985), in which an epidemiological profile of vitiligo in Calcutta was presented. Prevalence data were gathered from 15,685 individuals drawn from the general population; pedigree data were collected through 293 vitiligo patients. Overall prevalence of vitiligo is about 5 per 1,000 individuals (0.5%). There are no significant sex or age differences in prevalence rates. About a 4.5-fold increase in prevalence is observed among close biological relatives of affected individuals. The overall mean and modal ages of onset were about 22 years and 15 years, respectively. The mean ages among males (24.8 years) and females (19.3 years) are significantly different. In India, the incidence of vitiligo was reported to be between 1- 2 % The mean age at onset for males was found to be 23.3 years and for females was 17.4 years. (Majumder *et al*., 1988). A study was performed in a military service hospital (India) patient population utilizing 120 cases of vitiligo (Kar, 2001). The youngest patient in this series was a 2 year-old girl and oldest patient was 65 year old male. Vitiligo prevalence study in Shaanxi Province, China was also carried on the similar lines. The prevalence of vitiligo in Shaanxi Province was 0.093% (95% confidence interval, 0.067-0.127%). No significant difference was found between males and females or between urban and rural residents (Lu *et al*, 2007). Adults and children of both sexes were equally affected; however, the majority of the vitiligo cases are reported during stages of active development. About 50% of patients present before the age of 20 and nearly 70-80% present before 30 years of age. Although no age is immune to vitiligo, the disease is very rarely observed at birth (Abdullateef *et al.*, 2011). In Mumbai, India**,** records of 33,252 new patients attending a dermatology outpatient department were analyzed for the presence of vitiligo. A total of 204 (0.61%) were

affected by vitiligo. Male:female ratio was almost equal. Family history of vitiligo was seen in 3.43% of cases. (Poojary, 2011).

RESEARCH METHODOLOGY

The majority of the world's people remain outside of any kind of systematic health surveillance In the majority of countries where the burden of disease is highest, complete surveillance remains unrealistic or unaffordable (Beaglehole and Bonita, 2001; Setel *et al.,* 2006). This is more so in the developing nations like India. Population-based sample surveys and sentinel surveillance methods are commonly used as substitutes for more widespread health and demographic monitoring and intervention studies in resource-poor settings.

Unbiased sampling technique is essential for any kind of scientific enquiry. At the same time, no technique is totally free from bias. It should be necessarily biased towards what one is looking for in a sample. The percentage of people suffering from vitiligo varies from 1-4 as and there are no conclusive and accurate reports available now. Hence there is strong need to conduct a more accurate survey to find out the prevalence of vitiligo. There are a number of sampling techniques available, but none of them are fittingly suitable for the present survey. All the existing methods are governed either by chance or judgment (decision) of the investigator and hence none of these methods will give the exact picture of prevalence of vitiligo. In the present investigation a modified sampling method called Carpet Sampling Technique (CST) developed by Jayarama Reddy and Nayeem Ullah Khan (2013) was used. This method was designed to overcome the drawbacks of available sampling methods. CST was more or less suitable for the conduction of a survey to find out the prevalence of vitiligo in Bangalore city.

The steps involved in the collection of samples are as follows;

a) A questionnaire (Table 2) was carefully prepared with only a few questions so that there is active participation of people in the survey.

b) Volunteers were chosen and were given complete information about Vitiligo so that they can answer any questions raised by the people.

c) Each volunteer is asked to collect information from almost all people in the locality allotted to him or her. They were also asked to cover the entire area chosen by them. For example, if a college is allotted to one volunteer, he or she will collect data from all the students. This is the main feature of CST.

d) The data collected was carefully documented and used for further statistical analysis.

RESULTS

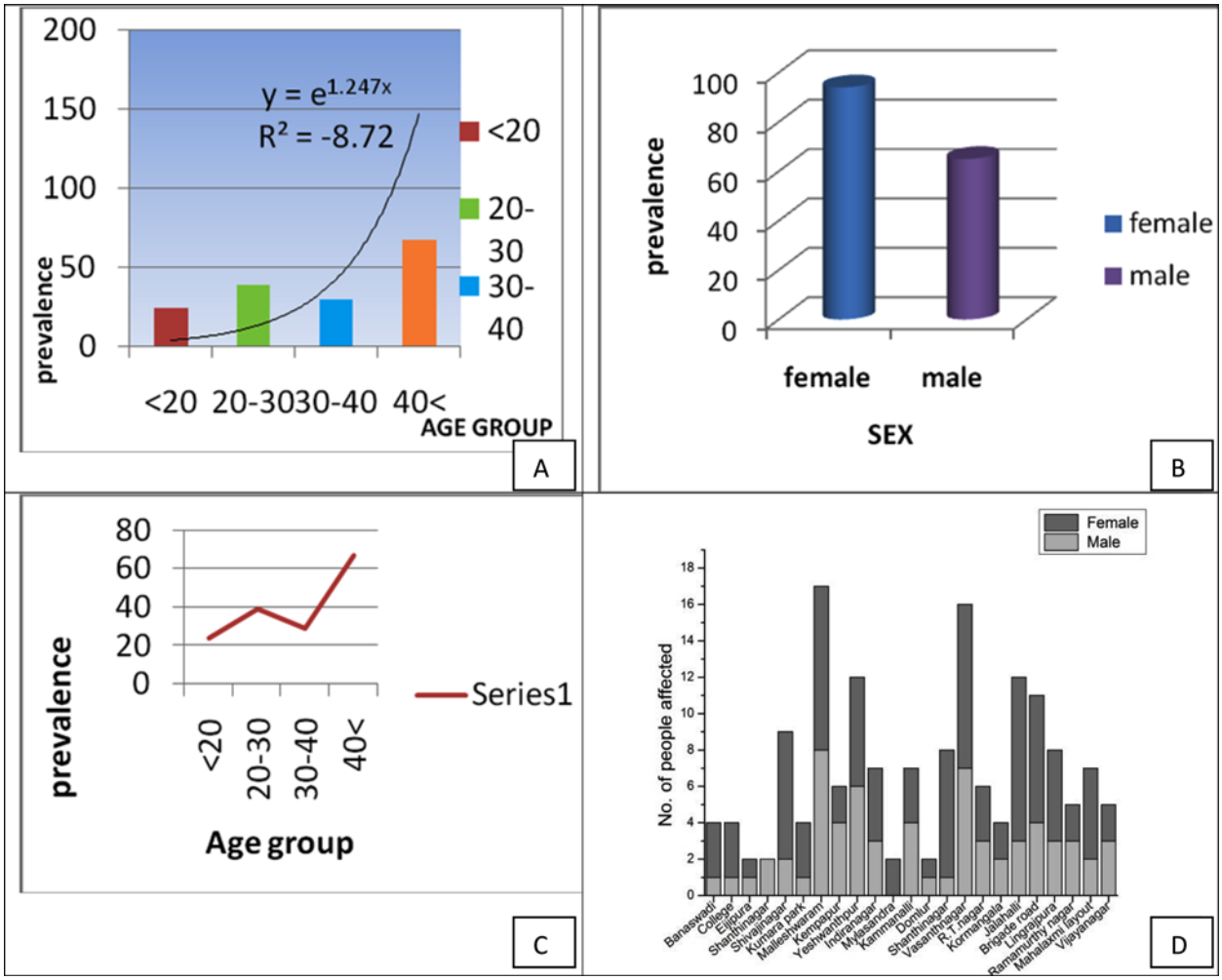
The incidence and prevalence of vitiligo in Bangalore was found to be 0.71% the details are given in the (Table 3). Some of the vitiligans obliged for photography and most of affected people did not like to be photographed and reluctantly participated in the survey. A total of 22037 people were contacted in the survey cutting across all segments of the society. A total of 160 people were found to be affected in the survey. Out of the total 160 people affected, 65 are males (0.29%) while 95 were females (0.43%). The age specific prevalence is 0.15% for people below the age of 20, 0.24% in the age group between 20 to 30 years, 0.18% in the age between 30 and 40 and was found to be increased to 0.42% in people

Table 3: Summary of the Survey Conducted In Twenty Different Localities of Bangalore City (Skin Colours: F-fair; B-brown; D-dark: %)

S. No.	Locality	No. of Participants	No. of Vitiligans	% in the Locality	Sex			Age in Years			Skin Colour		
					M	F	<20	20-30	30-40	>40	F	B	D
1	Banaswadi	452	04	0.6	1	3	1	-	-	3	-	3	1
2	St. Joseph's College	950	04	0.4	1	3	1	3	-	-	2	2	-
3	Eijipura	950	02	0.2	1	-	-	-	-	1	-	1	-
4	Shanthinagar	355	01	0.2	2	-	-	-	-	2	-	2	-
5	Shivajinagar	1012	09	0.8	2	7	2	-	5	2	3	2	4
6	Kumara park	1036	04	0.4	1	3	-	-	1	3	1	2	1
7	Malleswaram	1260	17	1.3	8	9	6	4	4	3	8	5	4
8	Kempapur	1004	06	0.6	4	2	2	3	-	1	4	2	-
9	Yeshwanthpur	1096	12	1.09	6	6	-	1	1	10	5	2	5
10	Indiranagar	1173	07	0.7	3	4	2	2	-	3	-	2	5
11	Mylasandra	1000	02	0.2	-	2	1	1	-	-	-	2	-
12	Kammanalli	938	07	0.74	4	3	1	-	-	6	-	4	3
13	Domlur	200	02	1.0	1	1	-	1	1	-		2	- -
14	Shanthinagar	1150	08	0.6	1	7	1	5	1	1	4	4	-
15	Vasanthnagar	1022	16	1.5	7	9	1	3	4	8	5	8	3
16	R.T.Nagar	1055	06	0.5	3	3	1	-	3	2	2	2	2
17	Kormangala	1000	04	0.4	2	2	2	-	1	1	-	2	2
18	Jalahalli	1038	12	1.15	3	9	-	1	2	9	5	7	-
19	Brigade road	1010	11	1.08	4	7	-	7	3	1	2	8	1
20	Lingrajpura	1006	08	0.79	3	5	1	1	1	5	3	5	-
21	Ramamurthy nagar	580	05	0.8	3	2	2	1	1	1	3	1	1
22	Mahalaxmi layout	1750	07	0.4	2	5	-	5	1	1	5	1	1
23	Vijayanagar	1000	05	0.5	3	2	-	1	-	4	-	4	1
		Total participants 22037	Total Vitiligans 160	Final average 0.71%									

above 40 years. There is also a significant difference in the frequencies of people with different skin complexions. 0.34% people with fair skin were affected while 0.45% of brown skinned people and 0.21% of dark skinned people were affected. No significant difference was found among people of different socioeconomic status. 83% (133 persons) of the vitiligans knew about

Figure 1: Tables: A - Graph Showing Age-wise Prevalence; B-sex-wise Representation of Prevalence; C- Graph Showing Increase in Rate of Occurrence With Rise in the Age; D-diagram Showing Prevalence in Different Locations of Bangalore (India)



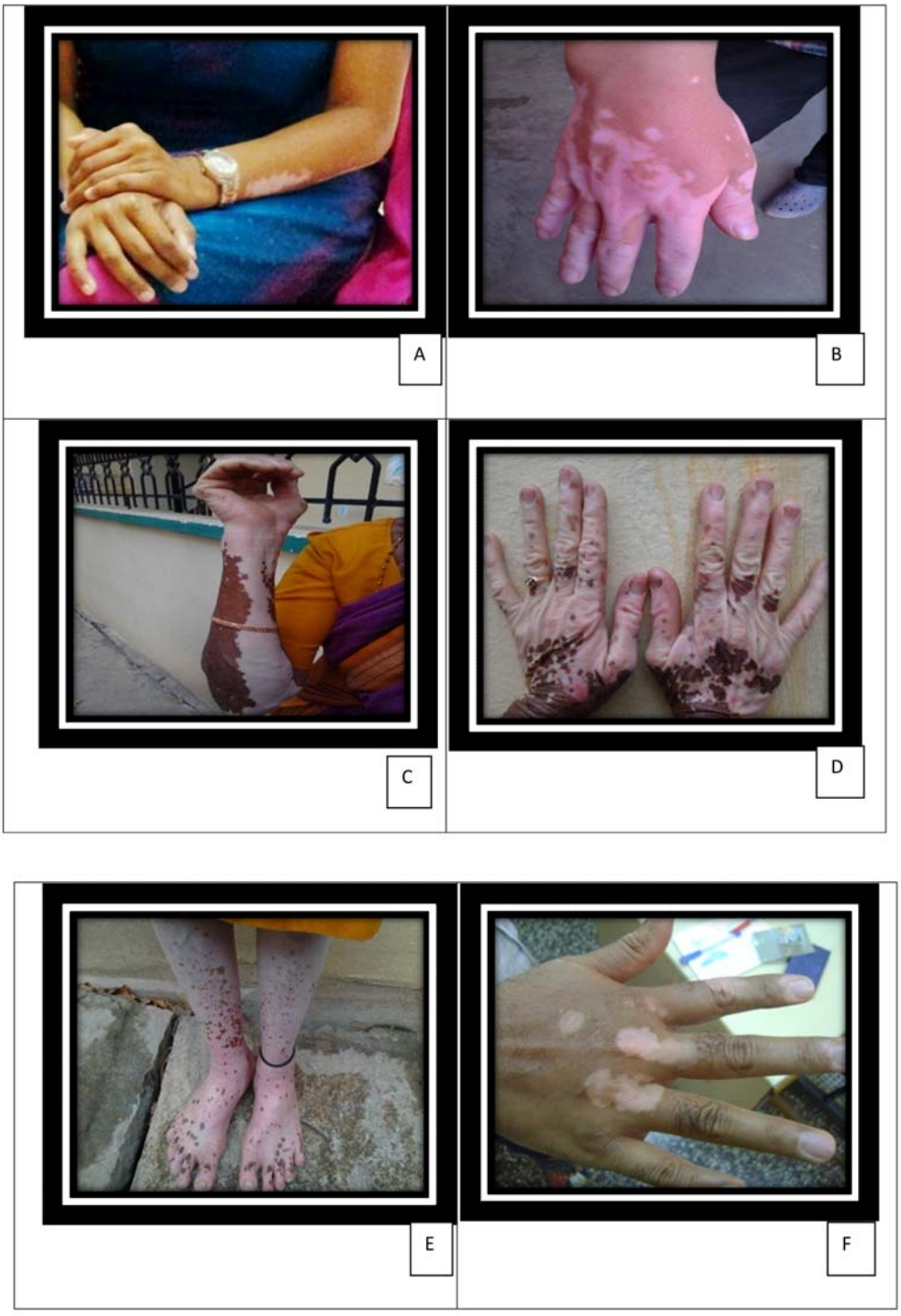
the problem and the others were not sure about the disorder. A question was asked to estimate the duration of prevalence of vitiligo and it was found to 1-25 years. It was revealed by the vitiligans that for conclusive appearance of vitiligo it will take 6-10 months. The manifestation is slow and gradual and it will first start as a tiny irregularly round dot and gradually spreads. Most common region of the body where it appears first was found to be face and closely followed by the hands. Contrary to the earlier reports regarding family history and hereditary factors, there was not even a single case to indicate that vitiligo is hereditary. In the survey it was recorded that 144 (90%) persons sought medical treatment and 80% of them were treated by Ayurvedic medical practitioners. It was also revealed that only two vitiligans showed a marginal improvement in the pigmentation followed by the treatment.

DISCUSSION

The percentage of people with vitiligo varies from 1 to 4 worldwide (Prasad *et al.*, 2003) and there are no conclusive and accurate reports available now. Hence there was strong need to conduct a more accurate survey to find out the prevalence of vitiligo. CST is a technique (Jayarama Reddy and Nayeem Ullah Khan, 2013) aimed at obtaining more accurate data as the rate of prevalence of vitiligo is low. The larger the size of the sample the accurate is the result and CST helped in this regard. However, even this method also has a drawback in being labor intensive. But it was still logical to use this technique for the sake of securing more accurate results. The strategies presented in this study relate to the level above the household level and data from all households and colleges within selected areas were collected once the area has been chosen. Even CST is not a totally unbiased method of sampling, as in any measurement process, a certain amount of error may be expected in routine population surveillance operations such as those in demographic surveillance surveys. Vital events are likely to be missed and errors made no matter what method of data capture is used or what quality control procedures are in place. The extent to which random errors in large, longitudinal datasets affect overall health and demographic profiles have important implications as it is the main platform for public health research and clinical trials. However, various parameters being measured and their distribution within the sampling unit of interest may not all be best represented by a particular sampling method.

The surveys reveal the fact that there is a difference in percentage of the prevalence of vitiligo in different parts of the world. However it is found to be around 1%. It is 0.38% in Denmark, 0.93% in China and 0.5% in Calcutta. Whereas, in Bangalore it was found to be 0.71%. There is significant difference with respect to the age groups but not with respect to socioeconomic groups. It is revealed by age wise analysis that the rate of incidence is higher in the age group of above 40. A similar report was given by Howitz. After the age of 70, the prevalence declined. This fall might reflect an increased incidence of vitiligo during the past few decades. The number of new cases of vitiligo increased steadily with advancing age, its onset being most often between the ages of 40 and 60 years (Howitz *et al.,* 1977).This clearly indicates that vitiligo is on the rise. The age factor is playing a role probably due to the fact that the appearance of vitiligo is late and its intensity increases with the progressing age. Hence the appearance of this disorder is low or minimal in the younger age group of people. The youngest patient was a 2 year-old girl and oldest patient was 65 year old male (Kar, 2001) and the disease was very rarely observed at birth (Abdullateef *et al.,* 2011). After the age of 70, the prevalence declined (Howitz *et al*., 1977). This is probably due to the fact that the incidence of vitiligo is gradually increasing. This is alarming and there is a need to develop or improve the existing methods of treatment. No significant difference was found between males and females (Das *et al., 1985:* Lu *et al.*, 2007). But in Bangalore out of the total 160 people affected, 65 are males (0.29%) while 95 were females (0.43%). This is significant due to the fact that females are not willing to reveal their skin disorder. There have been several theories with regard to the origin of vitiligo. Recent and modern studies have resulted in the understanding of the functional pathways. Its analysis has shown that most Vitiligo

Figure 2: Pictures of Vitiligans Who Were Involved In Survey Of The Prevalence Of Vitiligo Bangalore City (India). A- An Young Lady With Affected Arm; B-hand Of A Boy; C,D And E-an Old Woman With Vitiligo In Almost The Whole Body; F-appearance Of Vitiligo On The Hand



Susceptibility Ioci (VSI) encode immunoregulatory proteins or melanocyte components that are likely to mediate immune targeting and genetic relationships among vitiligo affected people. There have been major attempts to identify hereditary factors in vitiligo, and the genes identified to date support findings of Caroline Poole (contacted through e-mail, 2013) and her associates to support the fact that vitiligo is an autoimmune disease. However the causal gene still remains uncertain (Jin *et al.*, 2012). Lot of intensive research needs to done before finding any possible remedy for vitiligo. It is necessary to first of all understand the immune-genetic regulatory pathways in melanocytes.

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