Study of Susceptibility Towards Varicella by Screening for the Presence of IgG Antibodies Among Nursing and Medical Students of a Tertiary Care Teaching Hospital in Pune, India

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ABSTRACT

Background: It is believed that all suffer from chickenpox infection in their childhood. Many studies abroad and some in India clearly indicate that many individuals escape the infection in childhood, and thus, remain susceptible in adulthood. Adulthood chickenpox is a more serious infection than childhood. Prior screening of health care workers for the presence of IgG antibodies against Varicella will not only prevent hospital outbreaks but also economic and academic loss faced by the students. This will also have an important implication in terms of patient care as there is a threat of spreading Varicella to immuno-compromised patients. Definite history of prior infection of chickenpox is considered as an indicator for immunity towards the same. However, the reliability of this needs to be tested. **Aim:** A study to assess the susceptibility of nursing and medical students towards Varicella infection by screening for IgG antibodies against Varicella virus and to identify any risk factors for the same. Settings and design: A hospital-based cross-sectional study in nursing and medical students. **Materials and Methods:** Total 78 nursing and medical students participated in the study. They were given prestructured and pretested questionnaires. After obtaining informed consent, blood sample was collected and screened for the presence of IgG antibodies against Varicella by Enzyme Linked Immunosorbent Assay (ELISA) by using a commercial kit. Statistical analysis: Epi_info 2002 was used for analysis. Age of the study subjects were summarized as mean age and standard deviation. Susceptibility was analyzed as percentage with 95% confidence interval and Chi Square test was used to find association of susceptibility status with sex and region of residence in childhood. Relevance of definite history as an indicator for immunity was assessed by calculating sensitivity, specificity, positive and negative predictive values with 95% confidence interval. **Results:** Twenty males (25.6%) and 58 females (74.4%) participated in the study from medical and nursing students. The mean age ± standard deviation of mean was 19.4 ± 1.42 years for female students and 20.8 ± 2.13 years for male students. Total 20 (25.6%) students were found to be susceptible to Varicella with the confidence interval ranging from 15.8% to 35.4%. With respect to the gender of the students, the difference between the susceptibility percentage in female students (32%) and in male students (14.3%) was only a numerical difference and not statistically significant (χ^2 = 2.098, *P*=0.147, d.f. = 2). Also, the susceptibility was seen significantly more among Keralite students (Pearson Chi-Square=16.736, d.f=6, P=0.008; Likelihood Ratio=15.086, d.f=6, P=0.035; Fisher's Exact Test=13.569, p=0.022). The sensitivity of definite history of prior chickenpox infection as an indicator of immunity was only 55.17%, with C.I ranging from 43.9% to 66.4%, specificity was 80%, with C.I. ranging from 70.9% to 86%, and positive predictive value was 88.8% with C.I of 81.7% to 89% and negative predictive value of history of 66.6% with C.I. of 56% to 77.2%. **Conclusion:** Total 20 (25.6%) students were found to be susceptible to Varicella with the confidence interval ranging from 15.8% to 35.4%. Thus, there is a need for vaccination of all susceptible individuals. Definite history of prior chickenpox infection is not a reliable indicator of immunity against the same. The investigators recommend screening for IgG antibodies against Varicella of all students selected for the M.B.B.S. (Bachelor of Medicine and Bachelor of Surgery) and nursing course, and vaccination for susceptible individuals to prevent institutional outbreak and academic loss.

Key words: Nursing and medical students, Susceptibility, Varicella antibodies

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INTRODUCTION

Chicken pox is a highly infectious disease caused by Varicella (V – Z) virus. It has a high secondary attack rate from 70% to 90% among susceptible

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contacts.[1] It is assumed that almost all children suffer from chickenpox in their childhood. Varicella infection in adults is often more severe, prolonged with over 15 times more mortality than children.[1] Complications like hemorrhages, encephalitis, fetal wastage, and pneumonia are reported. Chickenpox can be fatal even in apparently normal adults.[2] The epidemiology of Varicella in the tropics is different from that in temperate regions. Seroprevalence patterns in a number of Asian countries indicate that seroconversion in tropical countries occurs at a later age than in temperate countries suggesting that tropical Asian countries may be at a greater risk of morbidity and mortality as a result of later-age seroconversion.[3] High ambient temperature, humidity, and high prevalence of certain other childhood viruses interfere with the transmission of Varicella virus.[2]

Although chickenpox in India is primarily a childhood disease, it is reported among adults especially Keralite adults.[4] Definite history of chickenpox is the usual method to assess the immunity against chickenpox. However, individuals and parents tend to forget about prior history as they grow older and reach adulthood. Thus, definite history alone cannot be a true indicator of immunity for chickenpox. Screening for the presence of IgG antibodies for Varicella virus is a useful method to assess the immunity against the same. Presence of IgG antibodies against Varicella indicates immunity, and conversely, its absence indicates susceptibility. Indirect immunoenzyme assay kit to test IgG antibodies against Varicella virus is available. As per studies conducted by the above method in tropical Asian countries, the susceptibility percentage was 21−35% in 15−20 years age group.[5-9]

There is limited number of studies from India. The susceptibility proportion in adults ranges from 14% to 30%.[10-12] All the above studies clearly indicate that the susceptible adult population is sizable. This holds true in case of health care workers. A susceptible health care worker can suffer from adulthood chickenpox with severe consequences. Alternatively, he can transmit the infection to hospitalized immuno-compromised patients.

The medical and nursing students because of their clinical postings and working and living in close vicinity with patients are constantly exposed to chickenpox virus. As per the study conducted in Christian Medical College, Vellore, South India there were 96 admissions for Varicella during the 1993−1997 period, and staff and student nurses accounted for 76%. The attack rate in staff and student nurses was 0.78 and 1.54 per 100 person-years, respectively. While community outbreaks of Varicella occurred in that region once in 4−5 years, hospital outbreak of Varicella occurred every year.[13]

Adulthood chickenpox also assume importance because of the academic and economical loss the sufferer faces due to period of isolation as its peak season being first six months of the year, which coincides with the examination period. Thus, there is a strong need to identify susceptible nursing and medical students.

The present study was therefore carried out to identify the susceptible individuals, and also to assess the reliability of definite history of suffering from chicken pox as an indicator for immunity against varicella.

MATERIALS AND METHODS

This was a hospital-based cross sectional study. The ethical clearance was obtained from the Institutional Ethical Committee. Inclusion criteria were all the students above 18 years, who did not receive Varicella vaccination in childhood and consented, were included in the study.

The exclusion criterion was acute illness, fever more than 38.5°C, recent administration of immunoglobulin, blood products, or immunosuppressive therapy. Since the study involved a blood collection procedure and a history of prior Varicella vaccination as exclusion criteria, the student response for participation was limited, and therefore, no sample size was calculated and instead purposive sampling technique was used. Thus, all students who fulfilled the selection criteria were included in the study. Indirect immunoenzyme assay kit to test IgG antibodies against Varicella virus is available. This test is affordable, widely available, and easy to perform and interpret.[14] This test has the sensitivity and specificity of about 98% and 97%, respectively.[15,16] The study subject were briefed regarding the nature of the study and after consent, the blood sample was taken under aseptic precautions. Serum was separated with centrifugation at 1500 rpm for 5 minutes immediately after blood collection and stored at −20°C until tested in the department of Microbiology. Enzyme-linked immunosorbent assay (ELISA) was used to measure VZV-specific IgG qualitatively. We used a commercial kit (VZV IgG CALBIOTECH INC, 10461 Austin DR, Spring Valley, CA). Serum samples were analyzed using the standard method as per the manufacturer's specification.[17] A pretested, prestructured questionnaire, which enquired for the basic information, vaccination history, history of any rash, definitive /doubtful history of chickenpox in the past was administered to the students. In case of doubt regarding the history of prior chickenpox infection, the

parents of the student were contacted for confirmation. The total duration of the study was six months.

Statistical analysis

Epi_info 2002 and SPSS-16 software were used for analysis. Age of the study subjects were summarized as mean age and standard deviation. Susceptibility was analyzed as percentage with 95% confidence interval and Pearson Chi Square test and Fisher's exact tests were used to find the association of susceptibility status with sex and region of residence in childhood. Relevance of definite history as an indicator for immunity was assessed by calculating sensitivity, specificity, positive and negative predictive values with 95% confidence interval.

RESULTS

Total 81 students took part in the study. Two blood samples were hemolyzed and one sample showed indeterminate status. Thus, only 78 students actually participated in the study. Out of 78 students, 15(19.2%) were M.B.B.S. students and 63(80.7%) were nursing students. Sex wise, 50 (64.2%) were females and 28 (35.8%) males. The mean age and standard deviation of mean was 19.4 ± 1.42 years for female students and 20.8 ± 2.13 years for male students. The study subjects were similar in socio-economic and educational aspects, and thus, only gender and area of residence during childhood were evaluated for possible risk factors. Only 36 (46.1%) students gave the definite history of suffering from to chickenpox in childhood in confirmation with their parents. A total of 20 (25.6%) students tested negative for the presence of Varicella antibody, thus making them susceptible for Varicella infection with the confidence interval of susceptibility ranging from 15.8% to 35.4%. Susceptibility proportion was more common in female students (32%) than male students (14.2%). This was only a numerical difference and not statistically significant (χ^2 = 2.098, *P*=0.147, d.f. = 2).

Region wise the susceptibility proportion was significantly more among Keralite students (66%) than other states (χ^2= 13.838 with 1 degree of freedom *P<0.000).*

The sensitivity of definite history of prior chickenpox infection as an indicator of immunity is 55.2%, with C.I. ranging from 41.6% to 68%. Specificity was 80%, with C.I. ranging from 55.7% to 93.4%. Positive predictive value was 88.9% with C.I of 73% to 96.4%. Negative predictive value of history of 38.1% with C.I. of 24% to 54.4%. The above figures are based on the assumption that the diagnostic test is perfect, that is 100% sensitivity and specificity. However, the sensitivity and specificity of our test is 98% and 97%, respectively. Thus, by applying the correction factor (0.98 and 0.97, respectively) the sensitivity and specificity is 54.1% and 77.6% [Tables 1-3].

DISCUSSION

In our study the susceptibility proportion was found to be 25.4% with a confidence interval of 15.8% to 35.4%. Gender wise, 16 (32%) were females and 4 (14.2%) males. Various studies in India quote the susceptibility proportion ranging from 14% to 30%.[8,11,12] Although the sample size is small, based on the confidence interval which ranges from 15.8% to 35.4%, even if we assume the lowest prevalence of susceptibility taken from the confidence interval (15.8%), it still reflects the threat for chickenpox outbreak. In a study at Christan Medical College Vellore, the attack rate in health care workers was more than that of the general population.[1] Another important finding of our study was the high susceptibility proportion among Keralite students (66.6%). As per White E in the study

Table 1: Gender wise distribution of susceptible individuals

Gender	Varicella antibodies present (%)	Varicella antibodies absent (%)	Total (%)
Male	24 (85.8)	4 (14.2)	28 (100)
Female	34 (68)	16 (32)	50 (100)
Total	58 (74.4)	20 (25.6)	78 (100)

χ^2 = 2.098 with 1 degree of freedom *P*=0.147

Table 2: Region/state wise distribution of susceptible individuals

Region/state	Varicella antibodies present (%)	Varicella antibodies absent (%)	Total (%)
Kerala	5 (33.3)	10 (66.6)	15 (100)
Maharashtra	10 (83.3)	2 (16.7)	12 (100)
Uttar Pradesh with Delhi	9 (81.8)	2 (18.2)	11 (100)
Punjab	10 (83.3)	2 (16.7)	12 (100)
Gujarat	8 (88.8)	1 (11.2)	9 (100)
Bihar	8 (88.8)	1 (11.2)	9 (100)
Others	8 (80)	2 (20)	10 (100)
Total	58 (74.4)	20 (25.6)	78 (100)

Pearson Chi-Square = 16.736, d.f = 6, *P*=0.008; Likelihood ratio = 15.086, d.f = 6, *P*=0.035; Fisher's Exact Test = 13.569, *P*=0.022

Table 3: Relation between history of chickenpox and susceptibility status

History of Varicella infection in past	Varicella antibodies present (%)	Varicella antibodies absent (%)	Total (%)
Definite positive history	32 (88.8)	4 (11.2)	36 (100)
Definite negative history	11 (45.9)	13 (54.1)	24 (100)
Doubtful history	15 (83.3)	3 (16.7)	18 (100)
Total	58 (74.4)	20 (25.6)	78 (100)

done in 1978, Chickenpox in Kerala was a notifiable disease with high mortality.[4] As per our study the susceptibility proportion among Keralite student is 66.6%. Thus, based on 95% confidence interval it appears that there could be a susceptibility proportion ranging from 42.8% to 90.5% in the general Keralite population. Even if we consider lower limit that is 42.8% it is still a very high susceptibility proportion considering the role of Keralite population moving out of Kerala in search of job or education. Thus, there are high chances of contracting chickenpox when going out of Kerala. However, why this susceptibility is still more needs to be investigated further.

Other researchers have found the sensitivity, specificity, positive and negative predictive values of self reported history for Varicella to be 87.2%, 83.2%, 94.3%, and 67.1%, respectively.[9] However, this was done in Singapore among military recruits. Thus, definite history alone cannot be a true indicator of immunity for chickenpox. This was also recommended by various workers.[12,13,17]

Chickenpox vaccine is very costly with two doses required as per the schedule for adults. Thus, the total cost of vaccination per person is approximately 3600 INR, i.e, 52.5 Euro or 77.4 USD. Testing the susceptibility using IgG antibody testing kit cost approximately INR 8000, i.e., 116.6 Euro or 172 USD and nearly 90 individuals could be tested with it. Thus, cost per individual would be 90 INR only, i.e., 1.3 Euro or 1.9 USD only. This is far less than the cost of the vaccine, and also to the academic and economical loss suffered by the student in case he/she suffers from chickenpox. Therefore, screening for the presence of antibodies against Varicella, and selective vaccination of the susceptible individuals is a cost effective method to prevent academic and economic loss and also to prevent hospital outbreaks.

Limitations of our study were a smaller sample size mainly because the procedure involved of blood sample collection. Thus, many students did not give consent. Another limitation was the proportion of nursing students was more in our study. This was due to the fact that more M.B.B.S. students had already received chickenpox vaccination in their childhood, and thus, were excluded from the study. This in turn led to increase in female subjects in the study. Further studies on a larger scale are required for confirming our findings.

All the susceptible subjects were told about their susceptibility status and were offered vaccination against chickenpox.

CONCLUSION

There should be a policy to screen all students opting for nursing and M.B.B.S. course for IgG antibodies against Varicella. A similar study should also be undertaken in general population too. Further a study to assess the impact of vaccination on prevention of outbreak in the students need to be undertaken, and depending on the results the strategy of vaccination should be undertaken to all health care workers. Vaccination should be offered to all susceptible individuals to prevent hospital outbreak, academic, and economic loss faced by the students.

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