

A Study of Recurrent Aphthous Ulcers in Sri Lanka

by

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SUMMARY Clinical presentation of recurrent aphthous ulcers of the oral cavity was studied in 1081 subjects. The overall prevalence was 23.5%. The age of onset was maximum during the second decade of life. 6% of the subjects had ulcers taking longer than 2 weeks for healing, suggesting that they suffer from major aphthae. The family histories were suggestive of an inherited susceptibility to the disease, although the mode of inheritance could not be worked out using the available data.

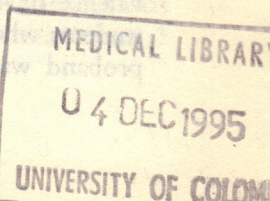
INTRODUCTION

Recurrent aphthous ulcers (RAU) form one of the commonest type of oral ulcers. They are persistently recurrent, painful ulcers of unknown aetiology, affecting the oral mucosa, which appear either singly or in crops and cause difficulty in mastication and speech. RAU usually appear on non-keratinized mucosa commonly affecting the buccal and labial mucosa and sometimes the specialized mucosa such as of the tongue. The shape of the ulcers depend on the site, and may be oval, round, elliptic or creatiform and have an erythematous margin. Three types of RAU are described: minor, major and herpetiform. Minor RAU are the most common, not exceeding 10 mm in diameter and heal within 7-10 days without scarring. The major RAU are usually over 1.5 cm in diameter, take over 2 weeks to heal and do so with scarring.

RAU have extensively been researched among the western populations (Gaykowski, Barlie, Lee and Stanley, 1966; Ship, 1972). However no data are available on the clinical aspects of this disease among the Sri Lankan population. The present study was undertaken to examine some aspects of the clinical characteristics of this common disorder and to study the hereditary tendency of RAU which has been reported (Ship, 1965).

MATERIALS AND METHODS

A total of 1081 subjects, including Peradeniya University students, and families of Dental Surgeons and students, were interviewed either directly or by means of a questionnaire to determine the prevalence RAU, the age and sex distribution, age of onset, recurrence pattern and the family tendencies.



The following clinical criteria were used to diagnose RAU (Axell, 1976) :

1. well defined, oral ulcers covered by greyish white or yellowish fibrinous exudate and surrounded by an erythematous halo.
2. location of lesions — in the non-keratinized mucosa or on the tongue.
3. presence of intense or moderate pain.
4. a past history of recurrence and healing.

Among the University students, the method of data collection consisted of interviewing the subjects by two examiners. All University students residing in two halls of residence (one male and one female) were examined. The dental students and surgeons who participated in the study completed a questionnaire giving relevant data on their family characteristics, identifying the members of family who either suffered from RAU at the time of the study or had a past history of RAU. A total of 188 questionnaires were distributed. All completing the questionnaire had prior knowledge of RAU, were acquainted with the disease and were instructed on the criteria for detection. Approximately 10% of those who responded were randomly selected to fill in the same questionnaire a second time to check the validity of the data supplied in the original questionnaire.

Segregation frequencies of autosomal dominant and recessive inheritance for RAU were determined from an equation based on the Hardy-Weinberg law (Stern, 1960) and the expected frequencies were calculated. A comparison of the expected and observed frequencies and ratios of RAU for different types of parental matings were made.

RESULTS

A total of 549 University students (including 133 Dental students) complied with the interviews. Of the 188 questionnaires distributed 108 were returned duly completed and providing data on a total of 623 family members.

A total of 309 subjects out of 1081 who participated in the study were afflicted by RAU at some stage of their life, giving a prevalence of 28.5%. Table I shows the distribution of RAU among the three study groups according to sex. The professionals (Dental Surgeons) had a prevalence of 56.5% and the University students a prevalence of 41.2%. Among the family members of the Dental Surgeons or Dental students who supplied the information the prevalence was found to be 14%, when the proband was excluded. Sex distribution among the afflicted subjects showed that

among the University students, the male to female ratio was 1:1.3, while among the total sample (which included all age groups) the ratio was approximately 1:1.6. Age distribution of the afflicted subjects was uniform until the age of 50 years and declined thereafter. Subjects below the age of 10 years were not represented in this study.

TABLE 1. Prevalence of RAU and distribution by sex

Sample	Female			Male			Total		
	Total	RAU +	%	Total	RAU +	%	n	RAU +	%
	n	n		n	n		n	n	
University students	362	162	45	177	60	34	539	222	41
Dental Surgeons	14	8	57	13	7	54	27	15	56
Family members	244	43	18	271	29	11	515	72	14
Total	620	213	35	461	96	21	1081	309	29

Age of onset of RAU was established in 122 subjects who revealed this information. The distribution by age is shown in Table 2. The onset of RAU was maximum during the second decade of life as reported by 57% of the sample under study. In less than 5% of the sample ulcers had first appeared after the 30th year.

TABLE 2. Age of onset of RAU in 122 subjects.

Age of onset	RAU +	
	n	%
0-10	31	25.4
11-20	69	57.0
21-30	16	13.1
31-40	5	4.1
41-50	1	0.8
51-60	0	0

Data on the frequency of recurrence of RAU was established among 240 subjects. Table 3 shows the frequency of recurrence among the afflicted group. It is seen that in more than half the sample a recurrence of oral ulceration occurs within every 3 months.

TABLE 3. Pattern of recurrence of RAU in 240 subjects

Frequency of recurrence	RAU+	
	n	%
Once in 2 weeks	7	2.9
Once in a month	40	16.7
Once in 2 months	21	8.8
Once in 3 months	63	26.3
Once in 4 months	44	18.3
Once in 6 months	42	17.5
Once a year	23	9.6

Duration of an ulcer or an ulcer crop before healing takes place was estimated among 102 subjects who were able to provide this information (Table 4). The large majority reported that their ulcers heal within ten days. However, in 6% ulcers took longer than 2 weeks to heal, and these subjects were identified as having major aphthae.

TABLE 4. Duration of an ulcer or a crop of ulcers in 102 subjects.

Duration (days)	RAU+	
	n	%
3-4	17	16.7
5-7	46	45.1
8-10	24	23.5
11-14	9	8.8
>14	6	5.9

In 75% of the afflicted subjects oral ulceration occurred in the buccal or the labial mucosa, while 10% reported ulcers on the tongue, with or without other sites being affected.

Among the University students, 45% of the Sinhalese and 38% of both Tamil and Muslim students reported to be affected by RAU. The difference among the ethnic groups was not statistically significant.

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Of the 108 probands who completed data on personal and family histories of RAU, 53 subjects (47.7%) presented a familial tendency with either one or more members being affected. The distribution of RAU positive offspring from various parental matings is shown in Table 5.

TABLE 5. Distribution RAU +ve and -ve offspring from various parental matings.

Type of mating	Parent pair n	Offspring			
		Total n	RAU- n	RAU+ n	RAU+ %
RAU- x RAU-	85	335	287	48	14
RAU- x RAU+	18	57	25	32	56
RAU+ x RAU+	5	15	2	13	87
Total	108	407	314	93	23

The percentage of offsprings affected with RAU was highest (87%) when both parents were affected, moderate when one parent was affected (56%) and lowest (14%) when neither parent was affected.

It was also found that when the person filling the questionnaire was negative for RAU only 3.1% of the parents were RAU +ve, while 35.6% of the parents had RAU among the positive probands.

The differences in the distribution of RAU +ve and RAU -ve siblings by sex were not significant. This finding excludes a possibility of an X-linked inheritance.

Assuming that a single pair of genes (alleles) forms the basis of inheritance of RAU, it is expected that 25% of the offspring would be affected in families where both parents are negative for the disease, if the pattern of inheritance is recessive. In this study only 14% showed RAU when both parents were negative (Table 5). This finding excludes the possibility of a recessive pattern of inheritance. Further, when comparison of expected and observed frequencies of RAU in siblings of three types of matings were made according to Hardy-Weinberg Law for recessive inheritance, it was seen that observed values for type I and II matings were higher than expected and for type III this value was lower than expected (Fig. 1). Thus, there is lack of evidence to support a recessive pattern of inheritance. Moreover, RAU is seen to be of high prevalence in the community. However, the number of family units with both negative parents are too low and therefore firm conclusions cannot be made.

For a disease showing a dominant pattern of inheritance, 100% of the offspring are expected to be affected when both parents suffer from it. In this study only 87% were afflicted when both parents were RAU positive. Further, when comparison of

expected and observed frequencies of RAU in siblings of three types of mating for dominant inheritance were made (Hardy-Weinberg Law) observed segregation ratios were lower than expected in all three types of matings (Fig. 2). These findings do not support a dominant pattern of inheritance for RAU, although this may represent a factor of incomplete penetrance.

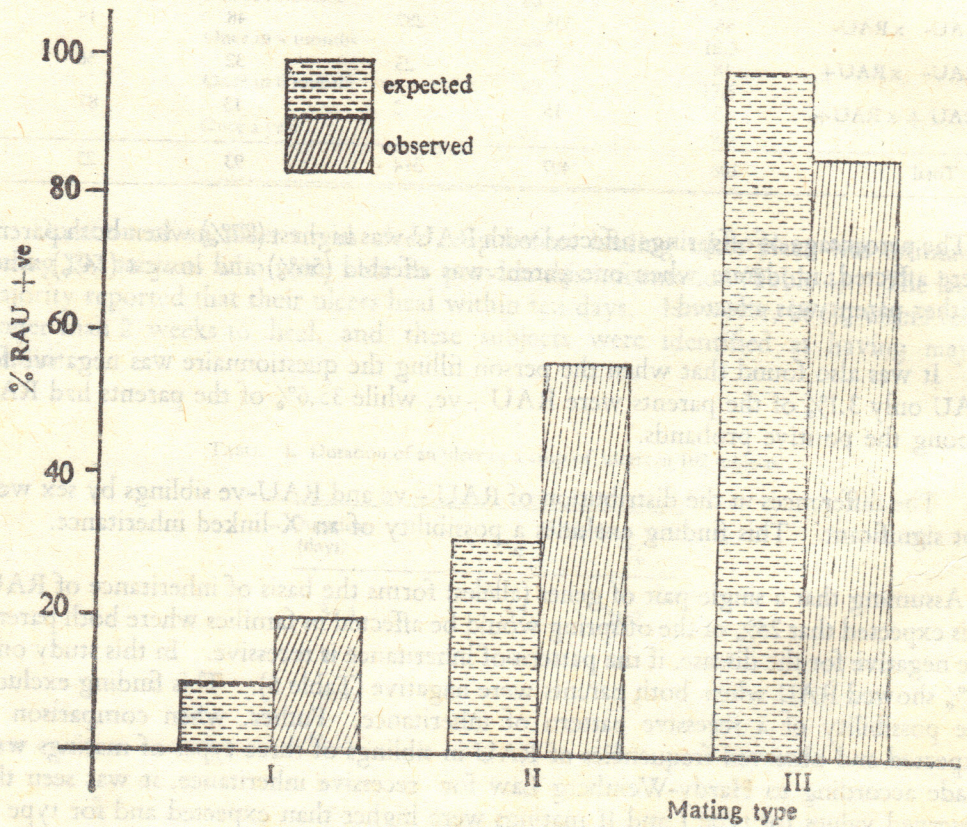


Fig. 1. Comparison of expected and observed frequencies of RAU in siblings of three mating types for recessive inheritance: Type I - Both parents RAU negative, Type II - One parent positive and one negative, Type III - Both parents RAU negative.

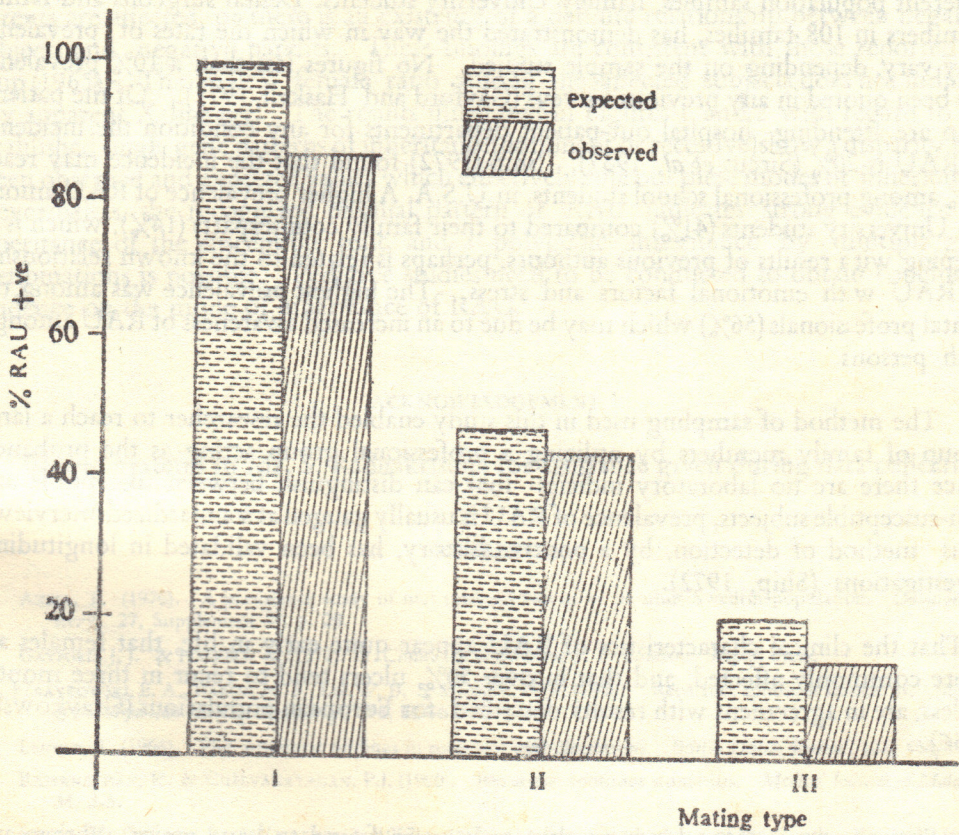


Fig 2 - Comparison of expected and observed frequencies of RAU in siblings of three mating types for dominant inheritance

- Type I - Both parent RAU -ve.
- Type II - One parent positive and the other negative.
- Type III - Both parents RAU positive.

DISCUSSION

Currently available data on the prevalence of RAU relate mainly to populations in the West. Further, the majority of these studies have been carried out among highly selected populations such as hospital outpatients (Sircus, Church and Kelleher, 1957) or using professional student groups (Ship, 1972). The present study, which deals with three different population samples, namely University students, Dental surgeons and family members in 108 families, has demonstrated the way in which the rates of prevalence may vary, depending on the sample studied. No figures less than a 10% prevalence has been quoted in any previous surveys (Gayford and Haskell, 1971). Of the patients who are attending hospital out-patient departments for any condition the incidence of RAU is 20% (Sircus *et al.*, 1957). Ship (1972) found that the incidence may reach 60% among professional school students, in U.S.A. A higher prevalence of RAU among the University students (41%) compared to their family counterparts (14%), which is in keeping with results of previous authors, perhaps is related to the known relationship of RAU with emotional factors and stress. The highest prevalence was among the dental professionals (56%) which may be due to an increased awareness of RAU amongst such persons.

The method of sampling used in this study enabled the researcher to reach a large group of family members by utilizing a professional group acting as the probands. Since there are no laboratory indices that can distinguish between susceptible and non-susceptible subjects, prevalence of RAU is usually gauged at standardized interviews. This method of detection, by a positive history, has been validated in longitudinal investigations (Ship, 1972).

That the clinical characteristics of RAU appear quite early in life, that females are more commonly affected, and that in over 50%, ulcers tend to recur in three months or less, are in agreement with results described for European populations (Graykowski, 1966).

Six percent of the subjects in this study were found to have major aphthae and this is closely similar to the findings by Lehner (1966) who reported an incidence of 8% in the U. K. However, among Malaysians, Ramanathan and Chelvanayagam (1980) reported that major aphthae occur in 29%. The clinical distinction of subjects afflicted by major aphthae is of importance because of their protracted course and the differences in management.

A positive family tendency for RAU susceptibility was found in 48% of the study population among the 108 families. This is consistent with the finding of Sircus *et al.* (1957), who reported a 46% family tendency, but low when compared with Graykowski *et al.* (1966). They described that 82% had an additional member or members of their family with a history of aphthae.

The results suggest that when both parents are affected by RAU the probability of the offspring being affected is very high and that it decreases proportionately when one parent or neither parent is affected by the disease. The fact that the negative subjects among those interviewed had only 3% of their parents afflicted with RAU may suggest one of two things: that either the negative subjects lack interest in the collection of correct data as compared with positive probands who reported that 35.6% of their parents are affected, or there is an existence of a definite relationship between negative subjects and negative parents. These findings are consistent with those reported by Ship (1965). The male: female ratio among the affected subjects does not indicate any apparent X-linkage. The results illustrated in Figures 1 and 2 with regard to the established single gene patterns of inheritance (dominant or recessive) show a disparity between observed and expected values which effectively rule out these modes of inheritance. Nevertheless, the recognized familial pattern of RAU indicates strong evidence for inheritance of the susceptible trait, and a polygenic inheritance by multiple gene combinations is possible. Pedigree studies need to be conducted to obtain conclusive evidence on the mode of inheritance of RAU.

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