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Periodontal status among relatives of aggressive periodontitis patients and reliability of family history report

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Abstract

Objectives: To assess the periodontal status of relatives of Aggressive Periodontitis (AgP) patients, and to evaluate the reliability of the family history report as provided by the proband.

Material and Methods: Data from 54 AgP patients were gathered along with a family history report for each of their relatives. Only 27 patients (probands) had relatives willing to be examined. This yielded a total of 61 relatives from whom the periodontal status was obtained. The family history report for each examined relative was compared with the periodontal diagnosis made at examination to assess reliability.

Results: Eight percentage of the examined relatives, aged between 12–76, were diagnosed with AgP, while chronic periodontitis was present in 39%, gingivitis in 38% and 15% were healthy. If the report provided by the proband was positive, the likelihood of finding any type of periodontitis in that relative was 85.7%, whereas if the report was negative the likelihood of the absence of periodontitis was 70.6%.

Conclusion: The percentage of examined relatives who were affected with AgP (8%), although lower than percentages reported in other AgP family studies, was still higher than the prevalence of the condition in random populations. Reliability of periodontal family history was considered good and more reliable when it was positive.

Key words: Aggressive Periodontitis; diagnosis; family history report; relatives; reliability

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Early onset periodontitis (EOP) represents a group of infrequent types of periodontal diseases that have their onset at a young age, with rapid attachment and bone loss which aggregate in families. The aetiology, although unclear, includes the sum of environmental (such as specific bacteria) and genetic factors. These heritable factors may pre-dispose to altered inflammatory or immunological processes (Michalowicz 1994, Diehl et al. 2003). The 1999 classification of periodontal diseases introduced a new term ''aggressive periodontitis'' to replace ''EOP'' to solve certain shortcomings of the previous classification (Armitage 1999). A patient would be diagnosed with AgP if he/she fulfils the three common criteria of rapid attachment/bone loss, being medically healthy and the presence of familial aggregation. The stringent age requirement used previously for EOP is no longer considered to be essential (Armitage 1999). However, despite attempts to improve the way we classify what we used to term EOP, there are still many uncertainties regarding the genetic aetiologic factor of this condition, as not only the gene/s involved are still unclear (Boughman et al. 1986, Hart et al. 1993), but even the mode of inheritance remains under discussion (Marazita et al. 1994, Michalowicz 1994, Hart & Kornman 1997, Tonetti & Mombelli 1999, Li et al 2004). In the same way, the familial aggregation feature of these conditions is taken for granted. However, if we examine the literature, we can see that the percentage of affected relatives of a given AgP/EOP patient or proband may vary from 8% in a group of affected Finnish families (Saxen 1980) up to 63% in one Brazilian family (Trevilatto et al. 2002). These different results cannot only be attributed to differences in the population, but to differences in the inclusion criteria, diagnostic criteria, the variable number of examined relatives (usually determined by self-selection bias) and obviously the number of families included. The largest segregation family study carried out, on

100 predominantly African-American families (Marazita et al. 1994), found a prevalence of more than 50% of examined relatives affected with EOP. However, the EOP diagnostic criteria differed between that selected for inclusion of probands and that for relatives with a lower attachment loss threshold chosen for inclusion of relatives.

In Europe, a recent study of one Scottish Caucasian family with a proband affected by Generalized EOP (Hodge et al. 2000) showed that from the 34 examined relatives, 41% were considered definitely affected with aggressive periodontitis, and a further 16% were probably or possibly affected. There is still a shortage of more extensive family studies of AgP in Europe and there are insufficient data in the literature which reflect the robustness of familial aggregation in AgP. On the other hand, the diagnosis of a periodontal patient may be uncertain (between the chronic and the aggressive form) and the reported family history may influence the clinician in classifying the patient one way or the other. However, the reliability of the report provided by the patient may often be questionable. The aims of this study are firstly to assess the periodontal conditions of relatives of AgP patients to ascertain the extent of periodontal breakdown within affected families and secondly, to assess the reliability of the periodontal family history report provided by the proband about their relatives.

Material and Methods

The Eastman Dental Hospital (London) is a referral centre for General Dental Practitioners (GDPs). All patients referred to the Department of Periodontology are first seen at a diagnostic New Patient Clinic. Those patients diagnosed with EOP/AgP are referred internally to an EOP/AgP clinic for further examination and data collection, and then allocated to either the School of Oral Hygiene or specialists in training under the care of the corresponding consultant. Ethical approval was obtained via the Eastman Dental Hospital and Institute Joint Research and Ethical committee.

Fifty-four AgP patients were identified at the Periodontology Department during 2001–2003 as fulfilling the criteria: to be diagnosed as Aggressive Periodontitis as outlined in the 1999 international classification system for periodontal diseases (Armitage 1999). These subjects met the clinical criteria for either localized or generalized aggressive periodontitis (Table 1), as described in the Consensus Report (1999), with the exception that familial aggregation was not taken into account. This was because family history was the factor being considered in this investigation. However, in order to be included in the study, the patient should have blood-related family members living in the UK and the patient should be willing to provide information about their blood relatives. All of these patients read the informative statement, gave consent to be included in the study and then filled out a questionnaire that included family details, ethnic origin, smoking status, medical status and specific information on signs of periodontitis for each of their blood relatives. This information was obtained from the patients without specific reference to their relatives, although the majority of the subjects had discussed their periodontal problems within their family. The patient had to state ''Yes'' or ''No'' for the presence of bleeding gums, mobile teeth, missing teeth or if they knew the blood relative had ever been diagnosed/treated for gum disease. This information was categorized as a positive, or negative report on each specific relative according to the criteria selected (Table 2). If the proband was uncertain about this information it was classified as dubious. The relatives' telephone numbers were also requested.

All relatives were given information (mainly via phone) about the study and our interest in examining them at the Hospital. On some occasions our invitation was declined because of phobia about dentists, being edentulous, having had previous periodontal treatment or not being able to attend (work, taking care of relatives or long/expensive trip to London). Those blood relatives who were older than 12 years of age and were willing to be examined were given an appointment. Once they arrived at the hospital they read the informative statement, consented to participate and underwent the examination. At a screening level, this consisted of an assessment of oral hygiene and gingival appearance (percentage of surfaces positive), a community periodontal index of treatment needs (CPITN) examination, using a WHO probe, and assessment of mobility and furcation involvement. If the overall CPITN score was 3 or 4 (at least one site showing probing depth >3.5 mm) a full periodontal charting was recorded (using a UNC15 probe) including probing depths, recessions and bleeding on probing at six points per tooth. The patient was then sent to the radiology department to have either a panoramic radiograph or a periapical radiographic series taken. In all cases, a hand-written report was given to the patient with the periodontal diagnosis and recommended treatment. The relative was advised to show this report to their GDP. In some cases, because of the periodontal condition, the recommendation was for the

Table 1. Diagnostic criteria for probands and relatives, based on the 1999 AAP Classification of Periodontal Diseases

Localized aggressive periodontitis
Rapid attachment and bone loss in otherwise healthy patients
First molar-incisor presentation with no more than two other teeth affected
At least two permanent teeth affected where at least 1 is a first molar
Lifetime cumulative attachment loss (LCAL) $\geqslant$ 4 mm on the affected sites
Generalized aggressive periodontitis
Rapid attachment and bone loss in otherwise healthy patients
Generalized interproximal attachment loss affecting at least three teeth other than first molars and incisors
LCAL $\geqslant$ 4 mm on the affected sites
Chronic periodontitis
Amount of attachment and bone loss is in relation to local factors
Most prevalent in adults
Usually slow to moderate progression
Gingivitis
Gingival inflammation present, but an absence of significant bone or attachment loss
Uncertain periodontitis diagnosis
Periodontal findings do not fit in any of the aggressive or chronic types of periodontitis
Edentulous
Patient lost all teeth
Healthy periodontium
Absence of gingival inflammation and attachment/bone loss in a dentate patient

GDP to refer the patient back to our Hospital.

Results

Only 27 out of 54 AgP patients had relatives willing to be examined. This subgroup of 27 AgP patients will now be termed Probands. The mean age at diagnosis of the proband group was 27.4, with an age range of 15–42, where 23/27 (85%) of these subjects were younger than 35 (Table 3). The majority of the probands reported being healthy 19/27 (70%), whereas the rest suffered from common conditions (asthma or allergy). The generalized AgP form was present in 17/27 (63%) of the probands and the predominant gender was female 22/27 (81%). Probands of white ethnic origin were more common 18/27 (67%) than from black origin 5/27(19%). However, black probands presented higher percentage of localized AgP than the white probands. 7/27 (26%) of the probands were current smokers 8/27 (30%) were former smokers while 12/27 (44%) had never smoked. Localized AgP probands presented a higher percentage of current smokers 4/10 (40%) than the generalized AgP probands 3/17 (18%). The demographic features that this group of probands presented followed the same trends observed in the original group of 54 AgP patients, with only minor differences (Table 3).

The proband group provided family history report on 137 relatives, from which 25/137 (18%) had a positive report and 54/137 (39%) had a negative report. The families of the 27 probands yielded 121 potentially available first degree relatives 12 years old or older. Periodontal status information (via examination or records) was gathered for only 59 of the 121 potentially available first degree relatives (49%). Sisters and mothers were the most likely group of relatives to accept our invitation to attend. Two more non-first degree relatives (one aunt and one uncle) were also added to the 59 described above, making a total of 61 blood relatives who were examined. The age range of these relatives at the time of diagnosis was 12–76 (mean 41), and 36/61 (59%) of them were female. The most common ethnic origin from the examined relatives group was white 43/61 (70%), followed by black 7/61 (12%), with the remainder 11/61 (18%) classified as other. The report previously provided by the proband about the relatives who were examined was positive for 14/61 (23%), and negative for 34/61 (56%) of them (Table 4). The periodontal status of the 61 examined relatives described previously was: chronic periodontitis in 24/61 (39%) of the subjects, gingivitis in 23/61 (38%), healthy periodontium in 9/61 (15%) and AgP in 5/61 (8%) (Table 5). Five out of 61 of examined relatives were diagnosed with AgPs. These five affected relatives with AgP came from five separate families. One of these AgP relatives was the mother of a proband, while the rest were siblings (three brothers and one twin sister) (Table 6). There was only one AgP relative of black origin and another of Indian-white origin; the rest were white. If we calculate the percentage of affected relatives among the examined relatives of these five families, we obtain a figure of 5/9 (55%) affected relatives. Those relatives diagnosed with localized ($n = 2$) or generalized AgP ($n = 3$) were from probands diagnosed with the same type of AgP. Chronic periodontitis was higher among examined relatives from generalized AgP probands 18/40 (45%) than from localized AgP probands 6/21 (28%). More Chronic Periodontitis cases were found among older relatives and more Healthy Periodontium and Gingivitis cases were found among younger relatives.

In the cases where the individual family history report was either positive or negative 48/61 (79%), this was matched to the subsequent diagnosis of the relative. If they coincided, the report was considered reliable. This occurred in 36/48 cases, equivalent to an overall reliability of 75% when the report was either positive or negative. Out of the positive reports, 12/14 (85.7%) were reliable as they were followed by diagnosis of periodontitis (AgP or chronic). Out of the negative reports, 24/34 (70.6%) were followed by diagnosis of healthy periodontium or gingivitis (Table 7). From the relatives who had a dubious report, 6/13 (46%) were diagnosed with chronic periodontitis. From

Table 3. Comparison of demographic data between the aggressive periodontitis (AgP) group and its subgroup the ''Probands''

	AgP patients		Probands	
	N	%	*N*	%
Total	54	100	27	100
Age range	15–42	–	15–42	–
Mean age at diagnosis	28	–	27.4	–
Females	38	70	22	81
White	31	57	18	67
Black	13	24	5	19
Asian	1	2	0	0
Oriental	2	4	0	0
Healthy	39	72	19	70
Generalized AgP	37	69	17	63
Current smokers	11	20	7	26
Never smoked	28	52	12	44
Total of reports on relatives	252	–	137	–
Relatives with +ve report	39	15	25	18
Relatives with –ve report	115	46	54	39

Table 2. Criteria for categorization of the reported family history, based on the information provided by the proband on each relative

Patient states
Positive report
Relative was diagnosed/treated with gum disease or . . .
Mobile teeth was present alone or in combination with bleeding gums/missing teeth
Dubious report
Relative lost all teeth or . . .
Unknown status of the relative or . . .
Bleeding gums present alone or in combination with missing teeth
Negative report
Denial of any sign of gum disease or . . .
Absence of any sign of gum disease but relative may have lost some teeth

Table 4. Demographic data on the blood relatives examined

	N	%
Total	61	100
First degree	59	97
Second degree	2	3
Females	36	59
White	43	70
Black	7	11
+ve report	14	23
Dubious report	13	21
− ve report	34	56
Age range	12–76	–

the relatives with positive individual reports, 2/14 (14%) failed to match with the diagnosis, as they presented with gingivitis only. From the relatives diagnosed with chronic periodontitis, 16/24 (67%) did not have a previous positive report, while only 1/5 (20%) of the relatives diagnosed with AgP did not have a positive report.

Discussion

The populations examined in this study were self selected and not random. The probands, were all patients diagnosed by their dentist as having severe periodontal disease who were referred to a specialist clinic, where a diagnosis of AgP was made. Similarly the relatives were blood relatives who were willing to be examined. Despite this ascertainment bias, the demographics of the population and their relatives are interesting. The large prevalence of females among the probands (70%) and relatives (81%) reflects a greater willingness for females to attend for investigations and/or treatment.

Only five out of 61 (8%) examined relatives were diagnosed with AgP. The proportion of AgP-affected subjects among examined relatives in our study is much lower than previously reported figures for EOP or localized juvenile periodontitis in USA. Marazita et al. (1994), in their (predominantly black) North-American population, found around 50% of examined relatives of EOP patients to be affected with the same condition. Other studies presented even higher percentages of affected relatives, but these were either examined relatives of only a group of selected families which presented already with at least one or more relatives affected (Hart et al. 1991, 1993), or described specific families, which presented an exceptionally high number of affected family members (Spektor et al. 1985, Hodge et al. 2000, Trevilatto et al. 2002). Therefore, they do not represent percentage figures of a random population. Our data are not truly random either, but we have included subjects regardless of previously reported family history. If we were to apply a similar selective approach to our data, and we exclude examined relatives from the 22 families, where no additional relative was found affected, we find that 5/9 (55%) of the examined relatives within these five selected families presented with AgP. However, if all the relatives within these families who were not examined proved to be free of AgP, the affected relatives would represent 5/26 (19%). Possible explanations for the difference between our 8% of relatives affected and the results from other studies (8%–63%) may be the use of different diagnostic criteria, possible ascertainment bias (probands and/or relatives), low number of examined relatives in our study and different geographical area/ethnicity mix. However, our 8% of affected AgP relatives is much higher than that reported in epidemiological studies such as the 0.1% of localized juvenile periodontitis subjects among a population of British school children (Saxby 1987) or the 0.66% prevalence of EOP in North-American young individuals (Loe & Brown 1991). Therefore, our result still supports the familial aggregation feature for the AgP entity. However, because of the modest number of affected subjects among the examined relatives in our study, we consider that the presence of familial aggregation among the principal features of AgP should be reviewed, or at least the absence of a reported positive family history should not preclude the diagnosis of AgP.

Chronic periodontitis was present in 24 out of 61 (39%) examined relatives. This finding is similar to results from other studies, such as 37% in Hart et al. (1993), and 36% of examined relatives in Boughman et al. (1988). Interestingly, examined relatives of localized AgP probands presented a lower percentage (28%) of relatives affected with chronic periodontitis in comparison with those from generalized AgP probands (40%). It is possible that some of the younger than 35-years old relatives, who at examination time were diagnosed with chronic periodontitis, could experience an increase in the rate of progression of the condition and develop an AgP.

The reliability of the family history report was calculated only when this was either positive or negative. A positive report was considered when the

Table 5. Periodontal diagnosis made for the examined blood relatives

Diagnosis	*N*	%
Localized AgP	2	3
Generalized AgP	3	5
Chronic Periodontitis	24	39
Gingivitis	23	38
Healthy periodontium	9	15
Total	61	100

AgP, aggressive periodontitis.

Table 7. Reliability of the report given by the proband on the relative: comparison of the report with the diagnosis made following examination of the relative (Dx)

Report on examined relatives	*N*	Matched by diagnosis (Dx)	% of reliability
Dubious	13	—	—
Negative	34	24	70.6
Positive	14	12	85.7
Total	61	36	
Positive or negative	48	36	75

Table 6. Description of the five families where additional relatives were found affected with aggressive periodontitis (Agp)

Proband diagnosis	Affected relative	Report for this relative	Diagnosis for relative	Age of relative	No of blood relatives potentially available	No of blood Relatives examined	Blood Relatives diagnosed with AgP
LAgP	Brother	+ve	LAgP	22	3	2	1
LAgP	Brother	+ve	LAgP	14	7	2	1
GAgP	Mother	+ve	GAgP	52	6	3	1
GAgP	Brother	− ve	GAgP	29	4	1	1
GAgP	Sister	+ve	GAgP	33	6	1	1
Total					26	9	5

patient informed us that this relative had been diagnosed/treated for any type of periodontitis or presented with wobbly teeth alone or in combination with other signs of periodontitis. A negative report was assigned when the patient categorically denied the presence of gum disease in this relative or the only information was some missing teeth. Relatives who were reported to be completely edentulous, were assigned a dubious report, as the reason for edentulism is often difficult to ascertain. Despite our effort to examine all available relatives, none of the edentulous relatives accepted our invitation. This could be explained by a lack of motivation, but also the advanced age of these patients and their less healthy status. The good reliability of the family history report provided by the patients and the low proportion of AgP cases among examined relatives in this study, has implications to planning health care services. We consider that AgP patients should be informed of the genetic nature of their condition and that other blood relatives could be at risk. Our results would suggest that the screening of relatives with a positive family history could be justified as a standard procedure, but negative family history reports are unlikely to yield significant numbers of affected relatives and may not be a justifiable use of scarce resources.

Conclusions

Collection of periodontal family history report from AgP patients about their relatives, and subsequent examination of their willing to participate relatives led to the following conclusions:

- Five out of 61 examined relatives (8%) were diagnosed with AgP. The prevalence of the condition among relatives of all our AgP probands, although lower than results from other studies, is still higher than in the general population.
- The report given by the proband was considered reliable. If the report was positive, it was followed by diagnosis of periodontitis in 85.7% of the cases, while if it was negative, periodontitis was absent in 70.6% of the cases.

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References

Armitage, G. C. (1999) Development of a classification system for periodontal diseases and conditions. *Annals of Periodontology* **4**, 1–6.

Boughman, J. A., Beaty, T. H., Yang, P., Goodman, S. B., Wooten, R. K. & Suzuki, J. B. (1988) Problems of genetic model testing in early onset periodontitis. *Journal of Periodontology* **59**, 332–337.

Boughman, J. A., Halloran, S. L., Roulston, D., Schwartz, S., Suzuki, J. B., Weitkamp, L. R., Wenk, R. E., Wooten, R. & Cohen, M. M. (1986) An autosomal-dominant form of juvenile periodontitis: its localization to chromosome 4 and linkage to dentinogenesis imperfecta and Gc. *Journal of Craniofacial Genetics. and Developmental Biology* **6**, 341–350.

Diehl, S. R., Wu, T., Burmeister, J. A., Califano, J. V., Brooks, C. N., Tew, J. G. & Schenkein, H. A. (2003) Evidence of a substantial genetic basis for IgG2 levels in families with aggressive periodontitis. *Journal of Dental Research* **82**, 708–712.

Hart, T. C. & Kornman, K. S. (1997) Genetic factors in the pathogenesis of periodontitis. *Periodontology 2000* **14**, 202–215.

Hart, T. C., Marazita, M. L., McCanna, K. M., Schenkein, H. A. & Diehl, S. R. (1993) Reevaluation of the chromosome 4q candidate region for early onset periodontitis. *Human Genetics* **91**, 416–422.

Hart, T. C., Marazita, M. L., Schenkein, H. A., Brooks, C. N., Gunsolley, J. G. & Diehl, S. R. (1991) No female preponderance in juvenile periodontitis after correction for ascertainment bias. *Journal of Periodontology* **62**, 745–749.

Hodge, P. J., Teague, P. W., Wright, A. F. & Kinane, D. F. (2000) Clinical and genetic analysis of a large North European Caucasian family affected by early-onset periodontitis. *Journal of Dental Research* **79**, 857–863.

Li, Y., Xu, L., Hasturk, H., Kantarci, A., De Palma, S. R. & Van Dyke, T. E. (2004) Localized aggressive periodontitis is linked to human chromosome 1q25. *Human Genetics* **114**, 291–297.

Loe, H. & Brown, L. J. (1991) Early onset periodontitis in the United States of America. *Journal of Periodontology* **62**, 608–616.

Long, J. C., Nance, W. E., Waring, P., Burmeister, J. A. & Ranney, R. R. (1987) Early onset periodontitis: a comparison and evaluation of two proposed modes of inheritance. *Genetic Epidemiology* **4**, 13–24.

Marazita, M. L., Burmeister, J. A., Gunsolley, J. C., Koertge, T. E., Lake, K. & Schenkein, H. A. (1994) Evidence for autosomal dominant inheritance and race-specific heterogeneity in early-onset periodontitis. *Journal of Periodontology* **65**, 623–630.

Michalowicz, B. S. (1994) Genetic and heritable risk factors in periodontal disease. *Journal of Periodontology* **65**, 479–488.

Saxby, M. S. (1987) Juvenile periodontitis: an epidemiological study in the west Midlands of the United Kingdom. *Journal of Clinical Periodontology* **14**, 594–598.

Saxen, L. (1980) Heredity of juvenile periodontitis. *Journal of Clinical Periodontology* **7**, 276–288.

Spektor, M. D., Vandesteen, G. E. & Page, R. C. (1985) Clinical studies of one family manifesting rapidly progressive, juvenile and prepubertal periodontitis. *Journal of Periodontology* **56**, 93–101.

Tonetti, M. S. & Mombelli, A. (1999) Early-onset periodontitis. *Annals of Periodontology* **4**, 39–53.

Trevilatto, P. C., Tramontina, V. A., Machado, M. A., Goncalves, R. B., Sallum, A. W. & Line, S. R. (2002) Clinical, genetic and microbiological findings in a Brazilian family with aggressive periodontitis. *Journal of Clinical Periodontology* **29**, 233–239.

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