VITILIGO: GENETIC LINKAGE ANALYSIS

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Abstract :

Since the familial aggregation of vitiligo has suggested a genetic role in the disease susceptibility and the conflicting results of the association studies with the ABO blood groups, we performed this study to clarify the possibility of an ABO blood group - linked control of the susceptibility to vitiligo.

Twenty four multi-case families were chosen for the study. The linkage analysis was performed by the computer program LIPED.

The highest Lod score (-0.08) achieved with a hypothetical dominant disease susceptibility gene with two alleles at a recombination fraction () 0.4 and penetrance rate 20%.

Introduction:

There are several arguments suggesting that vitiligo is a genetically dependent disease. The reports of extensive familial aggregation of vitiligo have suggested the important role of the genetic factor in the susceptibility to the disease[1-3]. A genetic model for this disorder proposed earlier postulates that recessive alleles at multiple unlinked autosomal loci are responsible for the premature death of the melanocytes[3]. Among the important genetic factors that have been studied are the ABO blood group antigens, but these association studies were rather inconsistent and conflicting[4-9] .

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Differences in the clinical features and HLA phenotype associations have suggested a heterogeneity in the pathogenesis between ABO blood groups and vitiligo was not tested before. This study was undertaken to clarify whether a genetic factor linked to ABO blood groups is involved in the pathogenesis of vitiligo with aggregation or not.

Material and Methods :

Twenty four multi-case families from the Arabian gulf region were chosen for the study. Selection of the families was based on the criteria that at least two siblings are affected with vitiligo and the availability of the parent for blood grouping. All members of the family were examined for any signs of vitiligo and typed for the ABO blood group. The ABO blood was carried out by the slide technique[11].

Linkage analysis was performed by computer program LIPED[12-13] which computes likelihood and Lod scores in a pedigree for given values of the recombination fractions and gene frequencies, based on the sequential test of Morton[14], (this involves the use of a maximum likelihood method a model is generated indicating which recombination fraction value is most likely to have produced the families observed) and utilized the procedure of Elston and Stewart[15], which calculates the likelihood recursively, starting with the most recent generation and working back to the most remote. The probability ratio of Haldane and Smith[16], provides the basis for calculating the values for examination with the sequential test of Morton[14]. This indicates the relative probability of the data given independent assortment, were the recombination fraction 0 is 0.5. This test is useful as it allows three decisions regarding data to be made ; if the total lod score is -2, no significant linkage exists between the two characters at the assigned recombination fraction ; if the total Lod score is or = +3, then significant linkage (p, 0.05) is established between the two characters at the assigned recombination fraction ; and if the total Lod score lies between -2 and +3 then linkage may exist between the two characters[14].

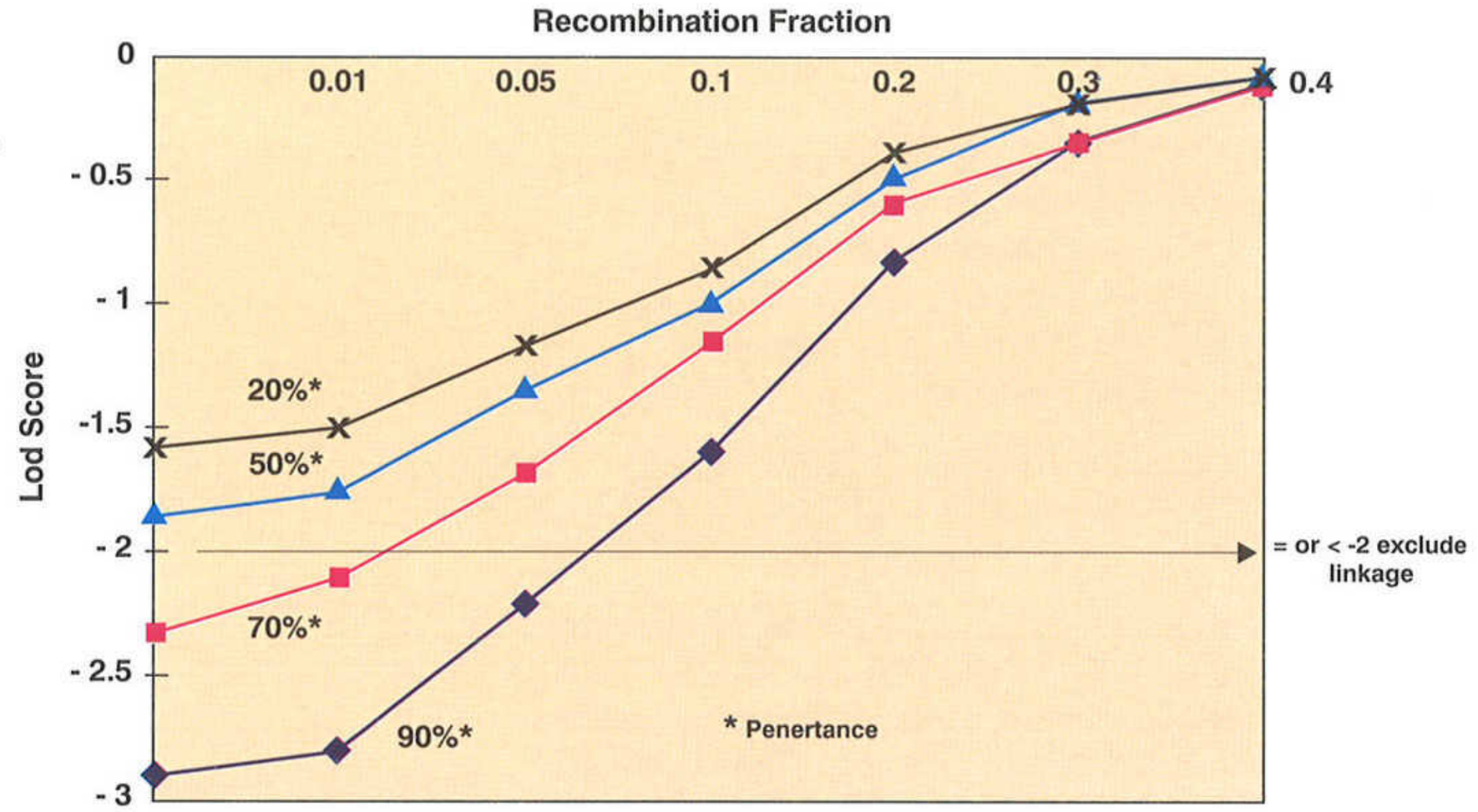

Fig.1: Lod score for two alleles with dominant inheritance hypothesis.

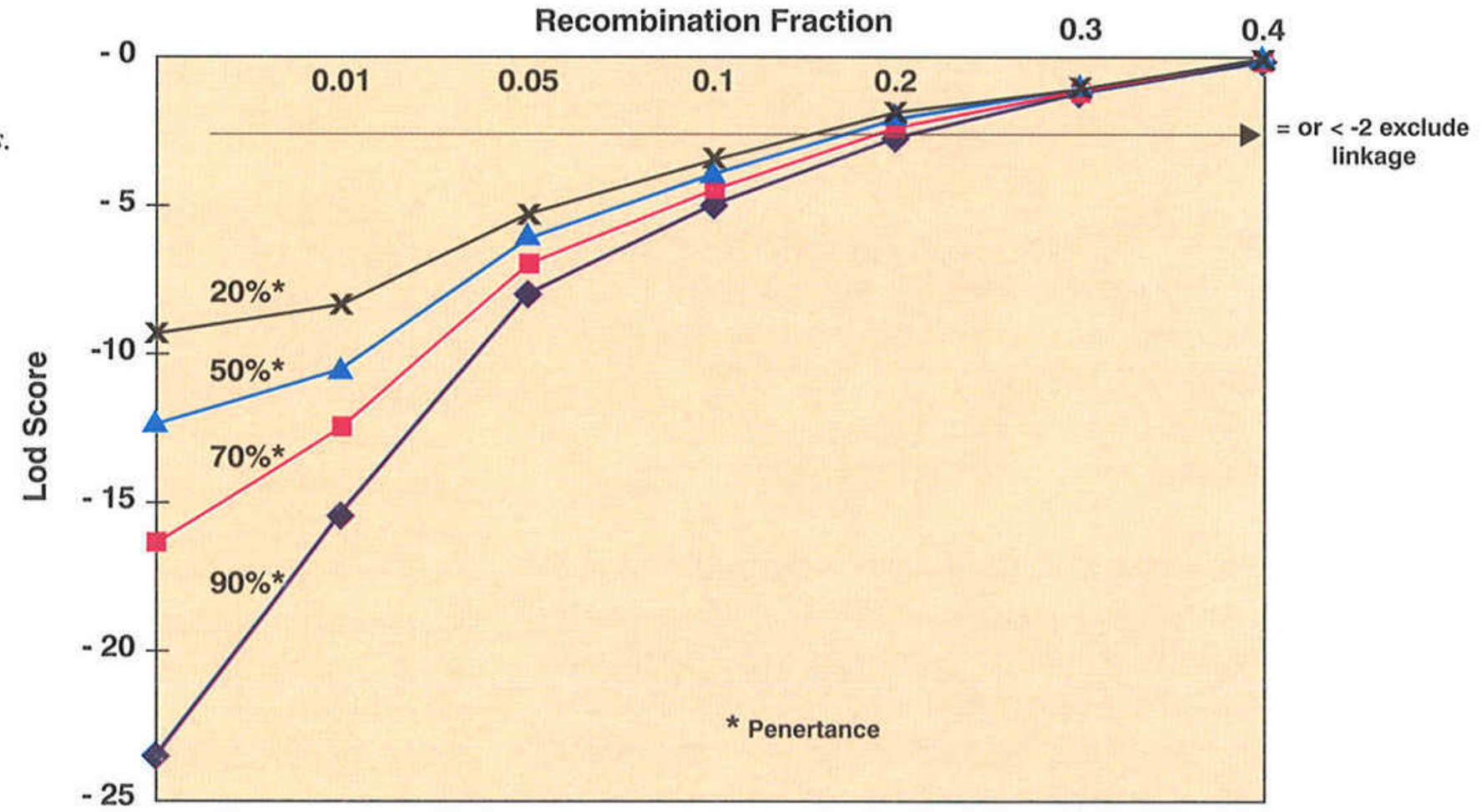

Fig. 2: Lod score for two alleles with recessive inheritance hypothesis.

Results :

Fig. 1 shows the Lod scores achieved from the linkage analysis between the ABO blood group and a hypothetical dominant disease susceptibility gene with two alleles. The highest Lod score was -0.08 at recombination fraction 0.4 and penetrance rate 20% for the disease susceptibility gene.

For the two alleles with recessive inheritance model (Fig. 2) the levels of Lod score were much lower than that achieved with the dominant inheritance model.

Discussion :

A familial aggregation of the disease has been extensively demonstrated which support the concept that genetic factors contribute to the etiology of

vitiligo[1-3].

Although a genetic model with multiple unlinked autosomal recessive alleles has been postulated in the pathogenesis of vitiligo[3], the highest Lod score (-0.08) achieved from our linkage analysis between ABO blood groups and susceptibility gene weakly linked (recombination fraction 0.4) to ABO blood group with dominant inheritance model and low penetrance rate (20%) remain to be identified and genetic linkage analysis against a panel of genetic markers may be necessary to reveal a more reliable linkage.

Conclusion :

A disease susceptibility gene weakly linked (= 0.4) to the ABO blood group with a dominant inheritance model and penetrance rate 20% is a remote possibility in the pathogenesis of vitiligo.

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