Amelogenesis imperfecta (AI) is a collective term for a group of hereditary defects of the enamel usually not associated with any other generalized defects. The etiology involves multiple mutations with varying modes of inheritance in genes critical for enamel development. The AI phenotype is broadly divided into hypoplastic, hypocalcified and hypomaturation types based on the stage of formation when the enamel was affected. It has been previously reported that AI can occur with distinct skeletal features including skeletal open bite and Class III malocclusion.

**Objective:** In this study, we asked whether the Class III trait is present in several pedigrees affected with AI. We hypothesize that skeletal Class III malocclusion occurs in a greater percentage of AI patients as compared with the general population (1-5%).

**Methods:** We therefore identified several large families with AI to examine the relationship between AI and skeletal Class III malocclusion. To initially diagnose the presence of skeletal Class III malocclusion, we performed cephalometric analyses for affected and unaffected individuals in 7 families focusing on, but not limited, to maxillary and mandibular unit lengths, overjet, and ANB angle. Pedigree analysis by inspection was performed to determine the inheritance pattern of skeletal class III malocclusion.

**Results:** Our cephalometric analysis revealed that a decreased ANB angle, decreased overjet and increased LFH was commonly associated with individuals in AI families. The Class III trait appeared to segregate in an autosomal dominant fashion. We further computed a relative risk for Class III in AI families of 19.42 (95%CI 12.1, 26.75).

**Conclusions:** Our results suggest that the Class III trait cosegregates with AI in our population, which represents an enriched sample for Class III malocclusion. Supported by NIDCR Grants DE12879 (JTW); RR-017442-04 (SAFB); and the AAOF (SAFB).