# MULTIPLE GNAS1, FGF23, FGFR3 GENES' STRIKING MUTATIONS IN CKD PATIENTS WITH SH. NEW BONE DISPLASIA-HEREDITARY OSTEODISTROPHY AND UGLIFYING HUMAN FACE APPEARANCES. SAGLIKER SYNDROME (SS).

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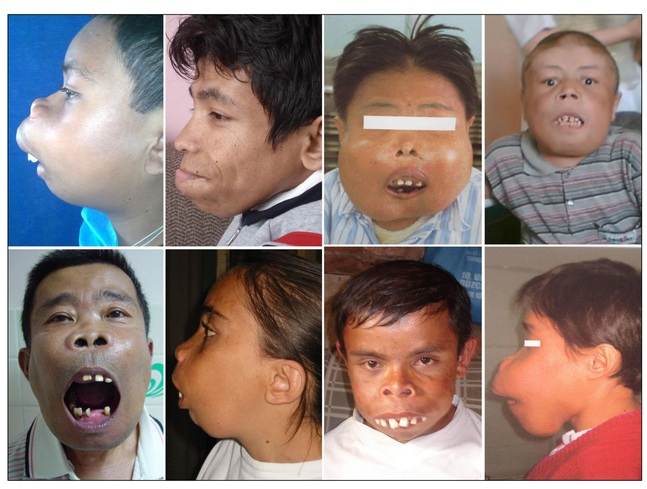
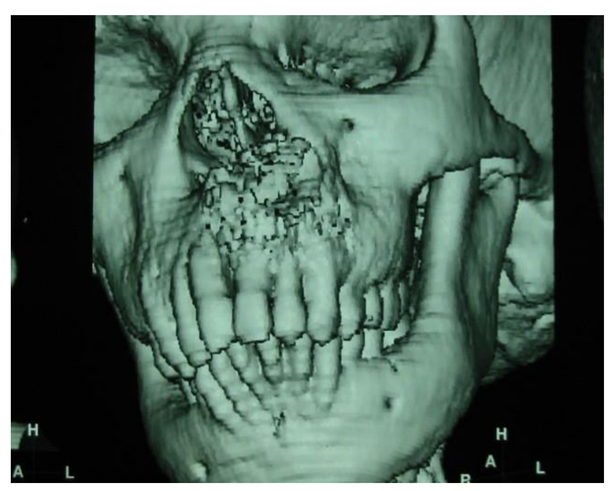
## INTRODUCTION

Sagliker Syndrome seems to be related to CKD and the consequent SH. SS starts and develops particularly before puberty while CKD reaches stage III level with overt SH. Since it occurs in some patients, it is plausible to think SS is genetically predisposed.GNAS1, FGF23 and FGFR3 genes' mismutations on the genesis of SS is unclear, and no data are available.

## METHODS

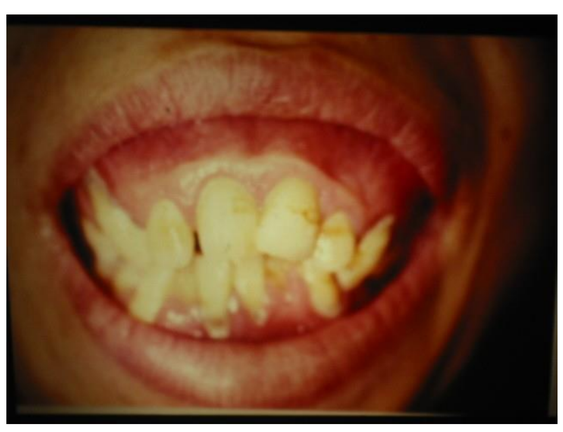
We conducted clinical, radiological, laboratory studies and screening for mutations in GNAS1 gene in 23 patients, FGF23 and FGFR3 genes in 17 patients.DNA isolations were performed from blood samples and mutations regions were amplified by Polymerase Chain Reaction (PCR).

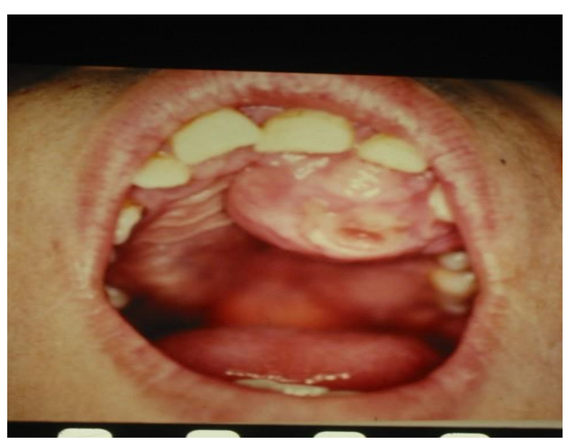


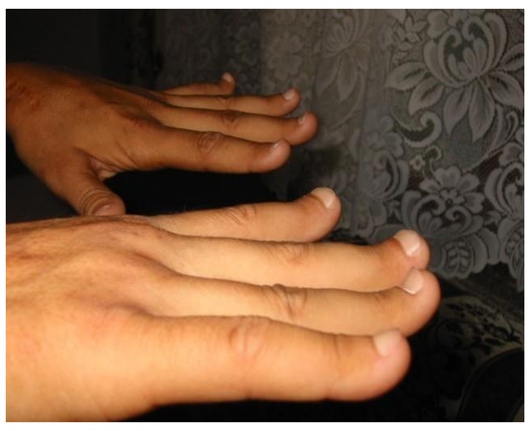


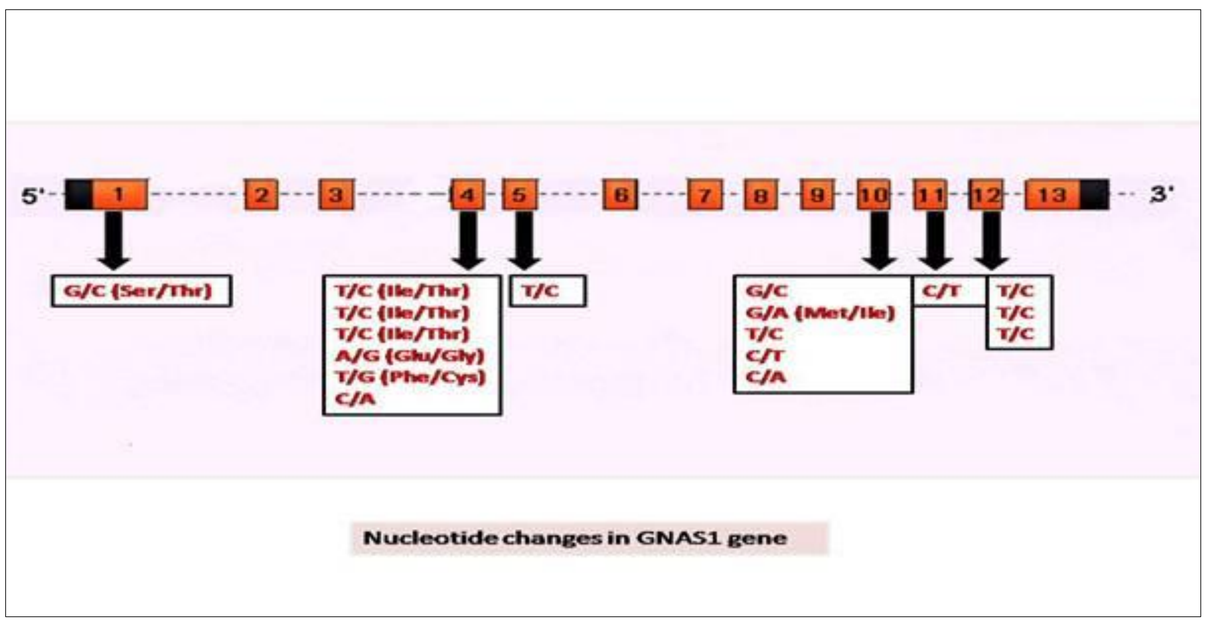

## RESULTS

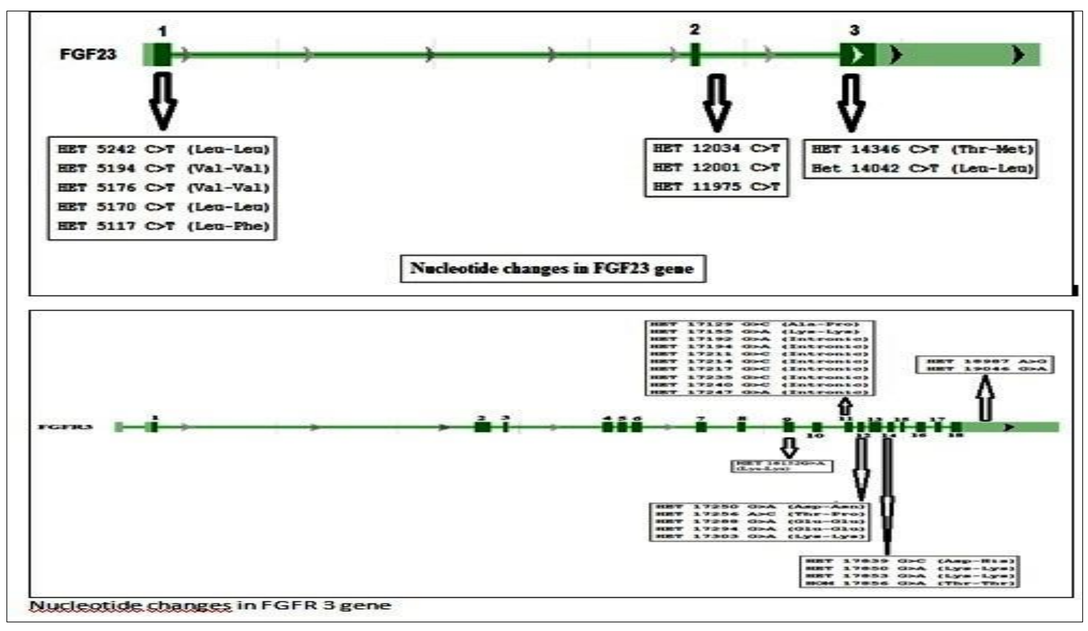
In 73.9% (17/23) patients, 17 different genetic abnormalities in GNAS1 were detected.Seven (58.3% ) of the 12 nucleotide alterations comprised novel missense mutations in different manners. There were also 6 heterozygous tranversion polymorphism in exons.Six of them were introngenic mismutations found in exons (introns; 65626, 70387 and 70817).We found 10 different mismutations in FGF23 gene. 8 were novel mismutations and are defined first in our study. 3 of them were in intronic region near exon 2.In FGFR3 gene we also found 22 different mutations. 16 were novel mismutations defined first in our study.8 of them were in intronic region near exon 11,last 2 were in non-coding exonic region of exon 18. Twelve mismutations were found in exons, 8 were found in introns and 2 were found in non-coding exonic regions. One was in the exon-exon junction region between exon 11 and 12 Therefore this mutation might be preventing splicing of this intron.










## CONCLUSIONS

There are plenty of mutations on those three genes in Sagliker Syndrome and are consistent with an insufficiency of those three genes playing a role in the clinical phenotype of loss of function mutations and with functional alleles having predominant roles in preventing the hormonal resistance.Since the incidence of CKD late stage III is around 8% in the world but the incidence of Sagliker Syndrome is around 0.5% in CKD patients, these gene mismutations might be responsible for bone Displasias-- Hereditary Osteodystrophies such as McCune-Albright syndrome, achondroplasias etc.., although our patients were not resembling any of them but they could be in between and Sagliker Syndrome might be a combination-compulsion of Bone displasias-Hereditary Osteodystrophies and SH and CKD.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