INTRODUCTION
Puberty is an important developmental stage for acquiring reproductive capacity. Different factors influence development of puberty. One of the genetic disorders is Kallmann syndrome in which hypogonadotropic hypogonadism and anosmia co-exist. Such cases are mostly diagnosed during adolescence due to the absence of secondary sex characters. This condition can be associated with a number of phenotypical abnormalities. Timely diagnosis and management can be highly beneficial. One such case is described hereby.

CASE REPORT
A 17-year-old male presented with short stature and generalized body weakness and aches since childhood. He achieved his milestones normally and was good in his studies. His parents were related and two of his brothers were also short statured.

On examination, his height was 130 cm and weight was 25.2 kg. He was pale and had anosmia which was verified by testing with different type of smells. He did not have any nasal blockage. Similar abnormality of anosmia was noted in his two siblings.

Despite being 17 years old, he did not have the normal pattern of facial hair growth, there was no change in voice, and testes were undescended.

Patient had decreased serum calcium and normal phosphate levels. Serum calcium was 8.4 mg/dl, serum phosphate was 4.6 mg/dl and Vitamin D3 was 15.1 ng/dl, which was markedly decreased. His serum testosterone was 0.06 ng/ml which was markedly low. Serum luteinizing hormone (LH) was 0.22 IU/ml and follicle stimulating hormone (FSH) was recorded to be 1.51 IU/ml. Both were lower than normal values. Serum prolactin level was normal i.e 4.9 ng/dl. Thyroid profile was normal. Insulin like growth factor (IGF-1) level was 45 µg/dl which was within the reference range. Insulin tolerance test was carried out. Post-test serum cortisol level was 7.6 µg/dl and human growth hormone level was 4.99 ng/ml. Both were lower than the expected response to hypoglycemia.

MRI scan of brain was performed. Hypothalamus and pituitary gland were normal. No abnormality was noted in area of olfactory bulbs and sulci. The patient was diagnosed to have Kallmann’s syndrome with Vitamin D, Growth hormone and central adrenal deficiency. He was put on replacement therapy including steroids, growth hormone and Vitamin D. Testosterone replacement is to be considered after achieving adequate growth hormone replacement.

DISCUSSION
Kallmann’s syndrome is a condition that specifies hypogonadotropic hypogonadism and anosmia. This clinical condition was first reported by Maestre de San Juan, a Spanish anatomist in 1856. Later, in 1944 an American geneticist, Kallman, reported a study of hypogonadism and anosmia occurring in three families. Hypogonadism is due to deficiency of gonadotrophin releasing hormone (GnRH) which occurs due to failure of the embryonic migration of neuroendocrine GnRH cells from olfactory epithelium to fore brain. Anosmia is related to the absence or hypoplasia of the olfactory bulbs and tracts in most of the cases.

The prevalence is reported to be 1 in 8000 in boys and about five times lower in girls. Some are sporadic but
most cases are familial as was noted in this patient. Three modes of inheritance have been reported: X-linked recessive, autosomal dominant and autosomal recessive. Five genes have been identified namely KAL1, FGFR1, PROK1, PROK2 and FGF8.

Usual presentation is due to abnormal phenotype including micropenis, loss of voice change, absence of definite hair distribution and infertility. Anosmia is usually noted on clinical examination. Different modes of presentation in addition to hypogonadism and anosmia have been reported. Hefner et al. reported 2 patients having Kallmann syndrome. One of the patients had skeletal pain due to osteoporosis along with loss of secondary sex characters, and the other was having symptoms of depression due to infertility. Jonklass reported a case of Kallmann syndrome associated with craniopharyngioma. Subramanian et al. reported Kallmann syndrome as one of the causes of short stature. This patient was short statured due to delayed skeletal development with absence of secondary sex characters. Cryptorchidism has also been reported in these patients as was noted in this patient.

Relevant investigations include serum testosterone levels which are low or absent. Luteinizing hormone (LH) and follicle stimulating hormone (FSH) are low. Other hormonal functions of anterior pituitary may be disturbed. Diminished cortisol response to insulin induced hypoglycemia has been reported. This patient also had decreased response of both cortisol and growth hormone. MRI scan of brain shows a hypo-plastic olfactory sulcus with absence of olfactory bulb in most of the cases. This patient’s MRI scan did not reveal any abnormality in olfactory area, a fact which has been reported by Subramanian et al.

Testosterone is given as part of replacement therapy to restore virilization and secondary sex characters. In females combined estrogen and progesterone are used. To restore fertility pulsatile treatment with GnRH can be used. Other treatment modalities are according to associated clinical problems. Counselling of patient and his family regarding the clinical condition and its management is also important.

Thus, it is necessary to diagnose Kallmann’s syndrome, as timely replacement can restore secondary sex characters and fertility. In this way, patient and his family can be saved from a lot of psychosocial problems.

REFERENCES