**Review of literature**

Thyroid disease is the medical situation with mal-functioning of thyroid gland. Among this disorder category, hyperthyroidism is that in which thyroid gland produces excessive amounts of thyroid hormones whereas hypothyroidism is that where thyroid gland does not produce enough thyroid hormone.\(^{(23)}\)

Galliford TM et al suggested that thyroid hormones are necessary for normal growth and preservation of bone mass in adults, although their mechanism of action in bone is not clearly understood. Decrease level of thyroid hormones lead to impaired bone development and growth retardation on the other hand, increase thyroid hormones cause accelerated growth, increased bone age and decreased bone mass. Osteoporotic fractures are more common in subjects with thyrotoxicosis or a suppressed thyroid stimulating hormone (TSH) from miscellaneous causes. Furthermore, in the thyrotoxicosis; bone loss is considered as the outcome of increased thyroid hormone acting on bones.\(^{(24)}\)

William JR stated that thyroid hormones are required for skeletal development and establishment of bone mass. There is retardation of growth and delayed development of bones in children suffering with hypothyroidism whereas accelerated maturation of bone in children with hyperthyroidism. Furthermore, in adults, thyroid hormones control metabolism of bone and BMD. Therefore, euthyroid status is essential to maintain optimal bone strength.\(^{(25)}\)

Gorka J et al. stated excess of thyroid hormones causes two fold increase of bone turnover resulting in net bone loss. These hormones may act directly on both osteoclasts and osteoblasts as receptors for thyroid hormones and TSH are present in bone. Hyperthyroidism affects more to a cortical bone rather than trabecular bone and is best measured by BMD at the distal forearm.
Hyperthyroidism increases the risk of fracture as the severity of hyperthyroidism is correlated with BMD.\(^{(26)}\)

In Contrast to this, Gonzalez RLA et al have found a high prevalence of hypothyroidism among adult postmenopausal females although no association between hypothyroidism and decreased BMD, vertebral or non-vertebral fractures was recorded.\(^{(27)}\) On the other hand Chin KY et demonstrated by quantitative ultrasound that there is a significant relation between strength of bone and TSH level.\(^{(28)}\)

Mundy GR et al demonstrated the effects of thyroid hormones are not only slower than those of other potent stimulators of osteoclastic bone resorption factors including osteoclast activating factors, parathyroid hormone, prostaglandins and vitamin D metabolites; but the maximum response is not as great. However T4 and Ts can directly stimulate bone resorption in vitro at concentrations approaching those which occur in thyrotoxicosis. Furthermore this effect may explain the disturbances of calcium metabolism seen in hyperthyroidism.\(^{(29)}\)

Reddy PA et al stated that thyrotoxicosis, a clinical syndrome characterized by increased level of thyroid hormones, which is one of the common diseases of thyroid gland. Thyrotoxicosis leads to increase rate of bone remodelling; which further causes the osteoporosis. Loss of bone density and elevation of markers of bone resorption is common in thyrotoxicosis. Moreover euthyroid patients with lower TSH values have been shown to have a lower bone density than those with high normal TSH.\(^{(30)}\)

C. Gennari et al revealed characteristics of osteoporosis include increased risk of fragility fractures, deterioration of bone architecture, and in addition to low bone mass.\(^{(7)}\) While Szabo ZS et al suggested hyperthyroidism is often associated with hypercalcemia which is provoked by osteoclastic activity of the
thyroid hormones.\(^{(31)}\) Alike, Dhanwal DK has shown thyroid hormones play an important role in bone mineral homeostasis and bone density. Moreover, favourably hyperthyroidism and, to some extent, hypothyroidism are related with decreased BMD which further leads to increased risk of fracture. However, majority of patients suffering with hyperthyroidism have concomitant vitamin D deficiency which aggravates bone loss.\(^{(32)}\) Safi S et al suggested primary hyperparathyroidism is a common disease, often asymptomatic. However severe primary hyperparathyroidism is associated with vitamin D deficiency.\(^{(33)}\)

Klaushofer K et al stated that thyroid hormones play a major role in the regulation of postembryonic or perinatal growth and development, including the functional differentiation of bone. Nevertheless, cellular events are the result of the interaction of T3 with nuclear receptors and, in addition, some extranuclear actions of T4 and T3. In response to the thyroid hormones, bone cells stop proliferation and develop differentiated functions. These include the production of growth factors, cytokines, prostaglandins as well as many structural proteins and intracellular messengers. Interactions with other systemic or local factors characterize the mode by which thyroid hormones regulate bone formation and resorption.\(^{(34)}\)

Nils K et al and Bjergved L et al have suggested that alterations in thyroid function, either with in the normal range, are associated with differences in BMI, caused by established minor variations in energy expenditure. This is more pronounced during the presence of mild hypo- or hyperthyroidism. Further, prevalence of such thyroid hormones abnormalities are high and may be associated with environmental factors. Although, TSH levels are not a determinant of future weight changes, and BMI is not a determinant for TSH changes, yet an association between weight change and TSH change is present.\(^{(35, 36)}\) On the contrary, Nyrnes A et al have revealed a significant association
between serum TSH within the normal range and BMI, both in a cross-sectional and a longitudinal study. \(^{(37)}\)

Thomas R and Silas C et al have suggested that moderate elevation of TSH concentrations associated with triiodothyronine (T3) values in or slightly above the upper normal range, is frequently found in obese humans. However, these alterations look like a consequence rather than a cause of obesity as weight loss does not cause normalization of elevated thyroid hormone levels. Moreover, investigators have demonstrated a statistically significant positive association between normal range serum TSH and BMI. No association was found between BMI and free T\(_4\) serum levels. \(^{(38, 39)}\)

Salamat MR et al and Kim SJ et al have shown that both BMI and weight are positively and significantly associated with BMD of hip and vertebrae. Furthermore, weight, BMI and BMD had a positive correlation. However, the coefficient of correlation between weight and BMD is higher than the coefficient between BMI and BMD, which indicates low weight, is much more expected to be associated to osteoporosis with no other factor considered. \(^{(40, 41)}\)

D’Eliaa G et al have suggested that there is increase of bones transparency by reducing trabesular bundles and cortical thickness in osteoporosis. \(^{(42)}\) While Salamat MR et al revealed that bone mineral absorbs much more radiation than soft tissue. The amount of X-ray energy which is absorbed by bone mineral calcium in one section determined the measured bone mineral content. Bone mineral content is divided by the area or volume of the bone estimates BMD. \(^{(49)}\)

Barbosa AP et al and Cammzi V have suggested that X-ray confirmed the BMD changes in post menopausal women and young men suffering with hyperthyroid may lead to the development of osteoporosis and vertebral fractures. \(^{(44, 45)}\) On the contrary Gonzalez-Rodriguez LA et al have revealed that
there is no relation between hypothyroidism and decreased BMD, vertebral or non-vertebral fractures. (46)

This is concluded that relation between thyroid disorders, BMD and BMI is still controversial. That is why the present study is designed to investigate the effects of thyroid disorders on long bones and vertebrae.