REVIEW OF LITERATURE:

Some obese patients may have hypothyroidism. Some studies strongly support existing, but contradictory evidence that serum TSH levels are positively correlated with the degree of obesity and some of its metabolic consequences in overweight people with normal thyroid function. Caloric needs due to hypothyroidism may be responsible for weight gain in these persons. In view of the strong association between hypothyroidism and obesity, it is advisable to look for hypothyroidism in these patients and screen accordingly through TSH testing and as hypothyroidism can affect cardiovascular system if not treated. Measuring cardiac marker like NT-proBNP can predict the risk of cardiac disorders. Thyroid dysfunction syndromes (hypo and hyperthyroidism) and obesity have major impacts on the cardiovascular system. Whilst the short term effects of thyroid dysfunction on the cardiovascular system are clinically obvious and well studied, the long term effects and particularly in relationship with obesity or BMI on the cardiovascular system remain unclear. Thyroid dysfunction syndromes (hyper and hypothyroidism) are known to affect the cardiovascular system in a number of ways. Whilst the acute effects of thyroid dysfunction on the cardiovascular system are more readily detectable especially with hyperthyroidism, the evidence on the long term effects of thyroid dysfunction on the heart and on the cardiovascular outcomes is less clear. This is particularly true of the mild or subclinical forms of hypo and hyperthyroidism. Measurement of serum or plasma BNP is being used increasingly in the clinical setting. In addition to ECG and X-ray examination, The Triage® BNP assay is the most widely used form of the BNP antibody test and is increasingly being used in Australia. The FDA-approved Biosite Triage® BNP assay is a point-of-care fluorescence immunoassay for quantitative assessment of BNP in whole blood or plasma EDTA samples. The first use of the rapid BNP assay in a clinical setting showed Patients with a confirmed diagnosis of CHF had a significantly higher mean concentration of serum BNP (1076±138 pg/ml) compared to those diagnosed with pulmonary disease (38±4 pg/ml, p<0.001). Synthetic BNP is also used as a treatment for heart failure, and therefore measuring BNP may not allow the physician to differentiate
between elevated BNP due to drug treatment or due to ventricular dysfunction. In a large sample of patients pooled from three European population-based studies of left ventricular dysfunction. Through multiple logistic regression analysis, which was adjusted for the higher levels of NT-proBNP in women and the increase in concentration of NT-proBNP with advancing age, showed that NT-proBNP was an independent predictor of CHF. Measuring NT-proBNP has a significant advantage over routine BNP—although the levels of the two will be same under ideal circumstances. NT-proBNP is more stable than BNP. The half-life of BNP is only 18-22 min. Additionally, once drawn, BNP levels are not stable in vitro for long periods, dropping significantly over the first 24 hours following collection. NT-pro-BNP is not biologically active, and has a half-life of approx. 60–120 min. But, NT-proBNP is dramatically more stable than BNP, with very little variation in the level of the marker after collection for at least 72 hours, and probably longer. So it can be assayed from stored or delayed specimens with confidence that the levels have not degraded with storage. As per the study published in journal Heart, on hospitalized patients with symptomatic and asymptomatic CHF highlights the utility of NT-proBNP in predicting Left Ventricle (LV) dysfunction NT-proBNP had a sensitivity of 73%, specificity of 82%, it also revealed that NT-proBNP has more diagnostic power to the clinical history. The physiologic actions of BNP are lowering of systemic vascular resistance and central venous pressure as well as an increase in natriuresis. Thus, the net effect of BNP is decrease in blood volume and a decrease in cardiac output. NT-proBNP levels in the blood are used for screening, diagnosis of acute congestive heart failure (CHF) and may be useful to establish prognosis in heart failure. Plasma concentrations of NT-proBNP are typically increased in patients with asymptomatic or symptomatic left ventricular dysfunction. In this context, there is no level of BNP that acts are an ideal cut off separating patients with and without heart failure. BNP accurately reflects current ventricular status.

The study titled ‘the impact of Thyroid dysfunction on cardiovascular risk’ showed the effect of thyroid dysfunction on N-terminal pro-B-type Natriuretic peptide concentrations, examines the changes in NT-pro-BNP in relation to hypo and hyperthyroidism. This study showed that treating hypothyroidism to euthyroid state is associated with a rise in NT-proBNP concentrations (p<0.001) and that treating
hyperthyroidism leads to a fall; however, this trend towards lower NT-proBNP levels in hyperthyroid group after treatment hardly reached statistical significance.

Changes in cardiac functions are observed in thyroid dysfunctions. Measured serum NT-proBNP levels by electro-chemiluminescence immunoassays shows that the serum NT-proBNP levels were higher in hyperthyroid patients than in hypothyroid patients. Some other studies using multiple regression analyses demonstrated that increasing free T4 was independently associated with a high serum NT-proBNP levels.

Serum NT-proBNP levels are higher in the hyperthyroid state as compared with the hypothyroid and euthyroid state. Thyroid dysfunction affects serum NT-proBNP levels, possibly influencing the secretion of the peptide. Therefore, thyroid function has to be considered when evaluating high serum NT-proBNP levels in patients without cardiac dysfunction. Hypothyroidism alters NT-proBNP concentrations. Serum NT-proBNP levels are affected by thyroid function due to the direct stimulatory effect of thyroid hormones. Two of the most common reasons for thyroid function testing are fatigue and obesity, but the vast majority of affected patients do not have hypothyroidism.

When BMI is divided into fat and lean mass components, a higher lean body mass and/or lower fat mass is independently associated with factors that are prognostically advantageous in CHF. Body mass index may not be a good indicator of adiposity and may in fact be a better surrogate for lean body mass in this population. Natriuretic peptides are known to play a role in obesity. Elevated body mass index (BMI) has been reported as a risk factor for heart failure. Prevention of heart failure through identification and management of risk factors and preclinical phases of the disease is a priority. Levels of Natriuretic peptides as well as activity of their receptors have been found altered in obese persons with some conflicting results. A study on Brazilian population depicts the involvement in severely obese patients and NT-proBNP and the correlation with the levels of these peptides in serum and plasma. They relate to BMI, duration of obesity, waist circumference, and echocardiographic parameters. However, NT-proBNP is increased in severely obese patients and its concentration in serum correlates with the duration of obesity. A per one such study indicates that a state of reduced natriuretic peptide level exists in the obese individual with heart failure. One
study proved that there in a significant relationship between TSH and lipid profile in obese patients. Therefore close watch of TSH is needed in those patients as they are prone for cardiac disorders. NT-pro BNP is regarded as a useful diagnostic tool for early detection of cardiac burden due to severe obesity. When adjusted for relevant co-variates, compared with normal counterparts, overweight and obese patients with acute CHF have lower circulating NT-proBNP and BNP levels, suggesting a BMI-related defect in Natriuretic peptide secretion. NT-proBNP fell below the diagnostic cutoff for CHF less often than BNP in overweight and obese individuals; however, when used as a diagnostic tool to identify CHF in such patients, both markers may have reduced sensitivity ,this is also been described 17.

A few studies showed that a substantial proportion of obese patients without CHF or CKD have concentrations greater than the upper reference limit for NT-proBNP but not for simultaneously measured BNP, similar explanation is been given by some other authors 18.

More recently some researchers showed measurement of NT-proBNP as an ideal cardiac bio-marker for the detection of impaired ventricular function as it satisfies several important criteria. It appears to be well-characterized, cardiac specific, easy to measure accurately and precisely (CV≤6.1%), and more stable in circulating blood compared to BNP .Some other also studies proved hypothyroidism decreases NT pro BNP concentrations and levels increase in hyperthyroidism 19.

Study explained the use of NT-proBNP to detect major-LVSD and major-SHD in patients with suspected HF could reduce referrals for specialist HF-assessment, provide cost-avoidance compared to direct referral and improve the efficiency of care 20

One researcher in his study explained that a single estimation of NT-proBNP at the time of hospital admission provides important information about LVEF in unselected patients 21

Certain studies strongly supports existing, but contradictory evidence that serum TSH levels are positively correlated with the degree of obesity and some of its metabolic consequences in overweight people with normal thyroid function 22.
According to the etiology of heart failure, some scientists found that both groups (ischemic and dilated) had a 65% decrease in NT-proBNP plasma levels in obese subjects compared to non-obese subjects.\textsuperscript{23}

Some study proved subclinical hypothyroidism is associated with an increased risk of CHF among older adults with age 70 to 79 yrs with a TSH level of 7.0 mIU/L or greater, but not with other cardiovascular events and mortality. Further investigation is warranted to assess whether subclinical hypothyroidism causes or worsens preexisting heart failure.\textsuperscript{24}

Results from several studies support the monitoring NT pro BNP for risk stratification of patients with CHF, with or without previous history. This involves patients presenting with a wide range of clinical pathologies including CHF.\textsuperscript{26, 27, 28}

Few studies examined the relationships between BNP and NT pro BNP in obese patients with and without CHF. For patients with CHF it has been described that increased BMI or obesity decreases BNP concentration. In non CHF patients decreased NT pro BNP decreases BMI in conjunction with therapy.\textsuperscript{29, 30}

Some tried to prove lower NT-proBNP plasma levels in obese heart failure patients when compared with non-obese patients.\textsuperscript{31}

Recent studies have suggested that NT-proBNP may be more accurate at detecting left ventricular dysfunction than BNP, as NT-proBNP is more stable and has a longer half life than BNP.\textsuperscript{32, 33, 34, 35, 36} Six studies investigated the diagnostic accuracy of the Elecsys® proBNP immunoassay compared to standard clinical assessment cardiography. The most salient finding from these studies was that NTproBNP testing has high negative predictive value (>92%), making it an excellent rule-out test in suspected cases. Patients suspected of having heart failure can then be selected for further investigation by echocardiography or other tests on the basis of having an elevated plasma concentration of NT-proBNP. If concentrations are normal, it is likely that symptoms
(dyspnoea, oedema) are due to other causes. The added value of an objective measure of NT-proBNP is that it identifies those at greatest risk of future serious cardiovascular events, including death. Normal concentrations of NT-proBNP virtually exclude diagnosis of CHF.

FT3 was the most powerful and only independent predictor of ICU mortality among the complete thyroid hormone indicators. FT3 had greater ability than NT-proBNP or CRP to predict primary outcomes. The FT3 levels were negatively correlated with CRP and NT-proBNP levels.  

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