relation between rs2268458 and rs2239610 genotypes and L-T4 dose or any of the studied biochemical and clinical parameters (Tables 4-5). A significant difference between the \( \text{THR}\alpha \) rs939348 genotypes and waist circumference (\( P=0.021 \)) was detected, where the TT genotype was associated with less waist circumference (Table 3). In addition, a significant correlation between L-T4 daily dose (mcg/kg/day) and the two alleles of rs939348 was found (\( P=0.014 \)), where T allele carrier patients required significantly higher doses of L-T4 for control of hypothyroidism (Table 3).

The patients were also divided into two groups based on current replacement L-T4 dose: low dose group (\( <1.7 \) mcg/kg/day, \( n = 154 \)) and high dose group (\( \geq 1.7 \) mcg/kg/day, \( n = 74 \)). The dose of T4 was associated with lower BMI (\( P=0.034 \)), WC (\( P=0.018 \)) and TSH (\( P=0.001 \)), and higher fT4 levels (\( P=0.001 \); Figure 1). Other parameters including age, presence of dyslipidemia, hypertension, diabetes mellitus, systolic and diastolic blood pressures, and the distribution of the genotypes of the three examined SNPs were not different between the two dosing groups.

**DISCUSSION**

In this study, we hypothesized that there might be an association between polymorphisms in the \( \text{THR} \) and \( \text{TSHR} \) genes and the replacement doses of L-T4. The role of thyroid hormones receptors (\( \text{THR}\alpha \) and \( \text{THR}\beta \)) in mediating the functions of the thyroid gland is well documented.\(^{16,17}\) In addition, thyroid gland functions are regulated by the action of TSH, which exerts its role through binding to \( \text{TSHR} \).\(^{21-23}\) Many studies have investigated the role of mutations in genes encoding \( \text{TSHR} \) and \( \text{THR} \) in the development of different thyroid diseases.\(^{5,24-26}\)

This study showed no association between \( \text{TSHR} \) SNPs rs2268458 and rs2239610, and the replacement doses of L-T4. Additionally, the current study found no correlation between these polymorphisms and the studied biochemical and clinical markers including thyroid function tests (TSH, fT3 and fT4). A previous study by Gu LQ and colleagues found that rs2239610 CC genotype was associated with higher serum concentrations of fT4.\(^{28}\) Another study by Louwerens et al. detected a modest effect for \( \text{TSHR}-\text{Asp727Glu} \) polymorphism on fatigue in patients with differentiated thyroid carcinoma.\(^{5}\)

In our study, we found a positive correlation between the \( \text{THR}\alpha \) rs939348 polymorphism and both L-T4 replacement doses and central obesity. On the other hand, our study showed lack of association...