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Molecular Characterization of DAT1 (SLC6A3) and *INF-γ* Genes Variants: Insights into Cancer Susceptibility in Egyptian Candidates

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Abstract

Genetic polymorphisms influence susceptibility to various diseases, including cancer and immune-mediated disorders. In this study, we investigated rs3836790 polymorphism in the dopamine transporter type 1 gene (SLC6A3/DAT1) and the *INF-γ* (+874 T/A) polymorphism in Egyptian women.

For SLC6A3 variant, Variable number of tandem repeat (VNTR) in intron 8 genotyping was performed using PCR to detect the common 5-and 6-repeat alleles. While INF-γ, the +874 T/A polymorphism was determined using allele-specific primers.

Our findings highlighted the variability of SLC6A3 intron 8 VNTR alleles within the study population, with the 5/ 6 heterozygous genotype being the most common. In parallel, the *INF-γ* +874 T/A genotype revealed diverse allele frequency pattern, suggesting a possible role in immune regulation and susceptibility to malignancy. Furthermore, allele distribution analysis showed trends of association with demographic parameters: the *INF-γ* A and SLC6A3 6-repeats mutant alleles were more frequent among younger women and women without cancer history. For the SLC6A3 VNTR, individuals carrying the 6-repeat mutant allele showed a tendency toward higher body weight compared to *INF-γ* A mutant allele showed a tendency toward lower body weight, indicating a potential link between dopamine regulation, metabolic control, and age-related changes. This study represents a baseline for future population genetics and disease-association studies SLC6A3 and *INF-γ* polymorphisms in Egyptian individuals. Larger-scale studies with extended sample sizes and detailed clinical correlations are recommended to validate these findings and to explore their translational relevance in medicine.

Keywords: DAT1; *INF-γ*; Polymorphism; SLC6A3.

1. Introduction

The dopamine transporter (DAT) is a member of the solute carrier 6 (SLC6) family that transports their substrates into cells through the transmembrane electrochemical gradient [1-3].

The main function of DAT is to remove DA from the synaptic cleft to the presynaptic neuron thereby limiting DA effects [4]. SLC6 depends on the energy from the sodium gradient which is maintained by the sodium/potassium ATPase pump. This electrochemical potential is used by DAT to accumulate intracellular DA in higher concentrations than outside the cell [2,3].

The human dopamine transporter gene *SLC6A3* (previously known as *DAT1*; genomic location: 5p15.33, 52,651 bases), has received substantial attention because it has been implicated in several diseases with a growing number of associated familial mutations [5]. It is also linked to inflammation [6,7], heart failure [8,9] and cancer [10,11]. The dopamine transporter gene mediates the re-uptake of dopamine in the synapses where vesicular monoamine transporter 2 sequester it into vesicles for storage and further release [12]. These mutations are relevant to diverse behavioral conditions including obesity that is considered a cancer risk factor. There is evidence for a relationship of SLC6A3 genotype to BMI in a small study in African Americans [13]. An association of a functional polymorphism at a key dopaminergic locus, the dopamine transporter (SLC6A3), and BMI was also confirmed in in American population [14].

Variable number of tandem repeat loci (VNTR) are important sites of genomic variation [15,16]. VNTRs

are defined as regions of DNA where a particular nucleotide sequence is repeated in tandem and the number of copies of the repeated sequence varies between individuals [17]. SLC6A3 has been studied extensively in relation to its VNTRs. SLC6A3 has 15 exons with ~52.5 kb length allocated on chromosome 5 (GRCh38/hg38: chr5:1,392,794–1,445,440). It contains a VNTR in the 39-UTR of the gene [18] with 3 to 11 repeat copy numbers and a consensus sequence of 40 bp in length.

VNTR intron 8 of SLC6A3 has repeat copy numbers of either 5 or 6, with a consensus repeat sequence length of 30 bp. This polymorphism has been associated with drug addiction in Brazilian individuals [19]. This intron 8 VNTR was also tested in many other studies for its association with disease related phenotypes.

Although SLC6A3 has received a large amount of attention in relation to its VNTR landscape and the associations of these VNTR alleles with phenotypes of interest, there have been both inconsistent and contradictory results reported.

Understanding SLC6A3's functional variants is required to delineate individual variation in DA-related pathophysiology and response to the environment [20,21]. To enhance our understanding, we performed a risk synthesis. Risk synthesis is not risk analysis, review or meta-analysis alone.

Interferon-gamma (IFN-γ) is a cytokine that plays an important role in innate and adaptive immunity. It activates macrophages and promotes cell proliferation, adhesion and apoptosis. It is produced by immune cells such as T cells, natural killer cells, and macrophage. As one of the main moderators of the immune response, IFN γ enhances the cytotoxic activity of NK cells and CTLs, which play a critical role in eliminating tumor cells, including those in MCC [22,23]. Additionally, IFN γ regulates macrophage polarity, recruiting them toward the proinflammatory M1 phenotype, [24]. Moreover, IFN γ increases the expression of MHC class I and II molecules on dendritic cells, to induce the sufficiency of T-cell responses and enhance the immune system's ability to recognize tumor-associated antigens [25]. SNP +874 T/A located at the 5' -end of a CA repeat at the first intron of human IFN-γ was found to be associated with many diseases [26,27]. These polymorphisms were potentially predisposing factors for many diseases. Knowledge of genetic background and marker may help elucidate the etiology and progression of diseases and is important in the intervention and management of the disease. Therefore, the aim of this study was to assess the association of genetic polymorphisms of dopamine transporter (SLC6A3 intron 8 VNTR rs3836790) and CA repeat allele (+874) in the first intron of the human interferon gamma gene with cancer disposition.

2. Subjects and Methods

2.1 Subjects

Forty-five female volunteers aged 25-52, with and without family history of cancer were included in this study. One of them was subsequently diagnosed with breast cancer and another one with a uterine benign tumor case (underwent tumor completely removed with surgery). These volunteers agreed to donate blood samples, personal and family cancer histories information for research purposes. This study was performed in compliance with relevant laws, institutional guidelines and the Declaration of Helsinki. It also was approved by the Faculty of Medicine Ethical Committee, Alexandria University (RB NO: 00007555-FWA NO: 00015712) [28].

2.2 DNA Extraction

Venous blood was collected from each participant in freezing tubes containing EDTA (anticoagulant). Genomic DNA was extracted from whole blood by using Thermo Scientific Gene JET genomic DNA purification kit (Thermo Fisher Scientific Inc. www.thermoscientific.com/onebio) according to the manufacturers' instructions.

2.3 Genotyping Methods

SLC6A3 rs3836790 variant Genotyping

Genotyping of VNTR variant in the intron 8 (rs3836790) was performed to detect the common 5- and 6-repeat alleles of the 30-bp tandem repeat. The fragment was amplified using the forward primer 5′-GCACAAATGAGTGTTCGTGCATGTG-3′ and the reverse primer 5′-AGCAGGAGGGGCTTCCAGGC-3′, as described by Moreau et al. (2015) [29].

PCR amplification was carried out in a final volume of 25 µL containing 1× PCR master mix (Bioline, Germany), 10 pmol of each primer (forward and reverse), and approximately 30 ng of genomic DNA. Thermal cycling conditions included an initial denaturation at 95 °C for 5 min, followed by 30 cycles of 94 °C for 40 s, annealing at 65 °C for 40 s, and extension at 72 °C for 2 min, with a final extension step at 72 °C for 10 min.

The resulting PCR products, which differ in size depending on the number of 30-bp repeats, were separated either on a 5% polyacrylamide gel or a 2% agarose gel stained with ethidium bromide. Bands were visualized under UV light, and allele sizes were compared to a molecular weight marker. Genotypes were determined as homozygous wild 5/5, homozygous mutant 6/6, heterozygous 5/6 and null (absence of two alleles) depending on the observed banding pattern.

IFN-γ +874 T/A (rs2430561) Allele-Specific PCR

The interferon-gamma (IFN-γ) +874 T/A

polymorphism, located at the 5′ end of the CA repeat region in the first intron of the human IFN-γ gene was detected using allele-specific PCR. Each reaction was carried out using a generic forward primer and two allele-specific reverse primers specific to the T or A allele [30]:

- Generic primer INF-(874) CP: 5′-TCA ACA AAG CTG ATA CTC CA-3′
- T-allele primer INF-(874) T: 5′-TTC TTA CAA CAC AAA ATC AAA TCT-3′
- A-allele primer INF-(874) A: 5′-TTC TTA CAA CAC AAA ATC AAA TCA-3′

PCR reactions were prepared in a 25 µL final volume containing 1× PCR master mix (Bioline, Germany), 10 pmol of each primer, and ~30 ng of genomic DNA. Separate reactions were set up for the T and A alleles. Thermal cycling conditions consisted of an initial denaturation at 95 °C for 5 min, followed by 30 cycles of 94 °C for 40 s, annealing at 56 °C for 40 s, and extension at 72 °C for 2 min, with a final extension step at 72 °C for 10 min.

Amplified fragments of 262 bp were separated on a 2% agarose gel stained with ethidium bromide and visualized under UV illumination. The presence of a band in the reaction with the T-specific primer indicated the wild T allele, while amplification in the A-specific reaction indicated the mutant A allele. Samples positive in both reactions were classified as heterozygous (T/A) [30] while samples negative in both reactions referred null (absence of two alleles).

2.4 Statistical analysis

Significant association between studied variants and each of age, weight, and cancer history of studied individuals were tested using the chi-square ($\chi 2$) goodness of fit Statistical Package for the Social Sciences (SPSS) version 22

(IBM Corporation, Armonk, NY, USA). p-values of ≤0.05 were considered significant. The P-values were predicted by Monte Carlo test.

3 Results and Discussion

With respect to SLC6A3 rs3836790, Int8 VNTR**,** results of PCR showed that there are four genotypes: homozygous 5/5 (wild), homozygous 6/6 (mutant), heterozygous 5/6 and null. The genotype 5/6 is the most common (46.7%)**.** Similarly**,** the most common genotype was a/t (37.8%) for IFN-gamma gene**.** The mutant genotypes (A/A) and (6/6) of both IFN-gamma and SLC6A3 genes, respectively, were less frequent than the wild genotype.

Association between Age and dopamine transporter (SLC6A3) Polymorphisms

The distribution of dopamine transporter (SLC6A3) intron 8 variant among age groups is presented in table 1& figure 1. Among participants < 40 years (n = 26), the most frequent genotype was 5/6 (46.2%), followed by the null genotype group (38.5%), mutant genotype 6/6 (11.5%), and 5/5 wildtype (3.8%). On the other hand, amongst participants aged ≥40 years (n = 19), the 5/6 genotype remained the most universal (47.4%), followed by the null (31.6%) then the wild 5/5 (21.1%); notably, none of this age group carried the mutant 6/6 genotype.

These findings indicate a predominance of the heterozygous 5/6 genotype across both age groups, whereas the mutant 6/6 genotype was restricted to the younger group.

The dominance of the 5/6 heterozygous dopamine transporter (SLC6A3) intron 8 variant has been consistently reported in other populations [31]. The absence of the 6/6 genotype in older individuals may be explained by sample size limitations or could suggest a possible age-related attrition of this allele, potentially reflecting reduced survival or increased disease susceptibility in carriers.

A higher prevalence of certain SLC6A3 variants has been associated with increased susceptibility to overeating, weight gain, and obesity-related metabolic changes, which in turn contribute to cancer development and progression [32-34].

In this context, the higher proportion of the 5/5 genotype among older individuals may indicate that this variant exerts a stabilizing or protective effect, potentially reducing susceptibility to obesity and cancer-related risk over time. Conversely, the restriction of the 6/6 genotype to younger individuals might reflect a risk-associated profile, with possible metabolic or oncogenic implications that limit persistence of this variant in later life.

These findings suggest that SLC6A3 intron 8 variants not only display age-related distribution patterns but may also contribute to pathways linking dopamine regulation, obesity, and cancer risk.

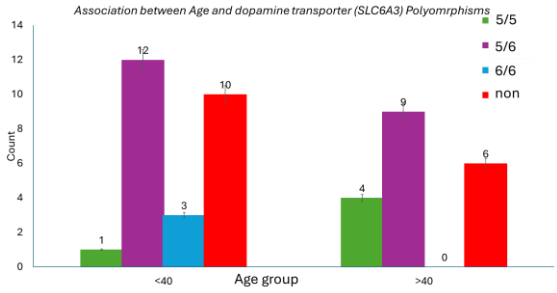

Figure 1. Association between Age and dopamine transporter (SLC6A3) Polymorphisms.

The chi-square analysis (Table 1) did not reveal a statistically significant association between age group and dopamine transporter (SLC6A3) intron 8 variants as predicted by Monte Carlo Test (p = 0.222). The lack of significant findings should be interpreted with caution. It is possible that the limited sample size (n = 45) restricted the ability to detect subtle genotype–age relationships. Moreover, the absence of the 6/6 genotype in older individuals may point to biological relevance that could not be captured statistically in this dataset. Larger number of samples would be required to clarify whether this pattern reflects a true age-related decline in specific variants or simply random variation due to small numbers.

Table 1: Chi square analysis of Association between Age and dopamine transporter (SLC6A3) Polyomorphisms

	Value	df	Asymp. Sig. (2-sided)	Monte Carlo Sig. (2-sided)		
				Sig.	95% Confidence Interval	
					Lower Bound	Upper Bound
Pearson Chi-Square	5.267[a]	3	0.15	0.20[b]	0.083	0.317
Likelihood Ratio	6.434	3	0.09	0.13[b]	0.034	0.233
Fisher's Exact Test	4.667			0.22[b]	0.101	0.344
N of Valid Cases	45					

a. 4 cells (50.0%) have expected count less than 5. The minimum expected count is 1.27.
b. Based on 45 sampled tables with starting seed 2000000.

3.2 Association between Cancer Hsitory and dopamine transporter (SLC6A3) Polymorphisms

The distribution of dopamine transporter (SLC6A3) intron 8 variants among participants with and without a history of cancer is presented in table 2 & figure 2. Individuals without cancer history (n = 28), have the most frequent genotype 5/6 (46.4%), followed by the null genotype (28.6%), 5/5 (14.3%), and 6/6 (10.7%). Individuals with cancer history (n = 17), have the 5/6 and null genotypes as the most common (47.1%), followed by wild type 5/5 (5.9%); notably, no carriers of the 6/6 genotype were identified in this group.

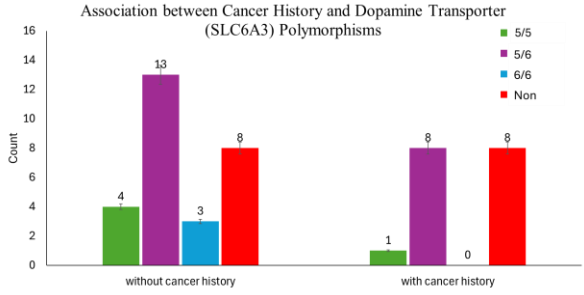

Figure 2. Association between Cancer history and dopamine transporter (SLC6A3) polymorphisms

Chi-square analysis (Table 2) showed no statistically significant association between cancer history and dopamine transporter variants as predicted by Monte Carlo Test (p = 0.444) and (95% CI: 0.299–0.590) confirmed these findings.

Table 2: Chi square analysis of Association between Cancer history and dopamine transporter (SLC6A3) Polymorphisms

	Value	df	Asymp. Sig. (2-sided)	Monte Carlo Sig. (2-sided)		
				Sig.	95% Confidence Interval	
					Lower Bound	Upper Bound
Pearson Chi-Square	3.511[a]	3	0.319	0.422[b]	0.278	0.567
Likelihood Ratio	4.572	3	0.206	0.422[b]	0.278	0.567
Fisher's Exact Test	2.979			0.444[b]	0.299	.0590
N of Valid Cases	45					

a. 4 cells (50.0%) have expected count less than 5. The minimum expected count is 1.13.
b. Based on 45 sampled tables with starting seed 2000000.

The results indicate that the heterozygous 5/6 genotype was the most frequent variant in both cancer and non-cancer groups, consistent with its overall predominance in the study population. Interestingly, the 6/6 genotype was completely absent in individuals with a history of cancer, while it was present in 10.7% of those without cancer. Although this difference did not reach statistical significance, it may suggest a potential protective role of the 6/6 genotype or alternatively reflect sample size limitations.

Another notable observation is the higher proportion of the null genotype group in cancer patients (47.1%

vs. 28.6% in non-cancer), which could indicate that the absence of polymorphism at this locus is associated with greater susceptibility to cancer. Conversely, the lower frequency of the 5/5 genotype in the cancer group (5.9% vs. 14.3%) may suggest a protective influence of this allele, though the small sample size prevents firm conclusions.

Given that the instability of Short tandem repeats (STR) can lead to pathogenic expansions, and have been linked to many diseases [35]. The severity of these diseases is reported to correlate with the size of the repeat expansion [36], the patterns observed here may reflect underlying biological mechanisms involving dopamine signalling in cancer susceptibility. Future studies combining genetic profiling with metabolic and clinical data would help clarify the role of SLC6A3 intron 8 variants in cancer risk.

3.3 Association between Weight and dopamine transporter (SLC6A3) Polymorphisms

The distribution of dopamine variants across weight categories (<70 kg vs. ≥70 kg) is presented in table 3 & figure 3. Among participants with weight <70 kg (n=10), the most frequent genotype was 5/6 as well as the null (40.0%) then 5/5 (20.0%), and no individuals carried the 6/6 genotype. In contrast, among those with weight ≥70 kg (n=35), 5/6 the most common variant (48.6%) was detected, followed by the null (34.3%), and both 5/5 and 6/6 genotypes were observed in 8.6% each. Overall, across all weight categories, the 5/6 genotype was predominant (46.7%), while the 6/6 genotype was least represented (6.7%).

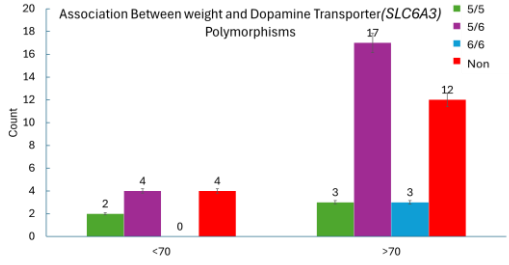

Figure 3. Association between weight and dopamine transporter (SLC6A3) polymorphisms

Chi-square testing (table 3) revealed no statistically significant association between weight categories and dopamine variants (Monte Carlo test p = 0.689).

The findings of this study indicate that dopamine gene variants were not significantly associated with weight status (<70 kg vs. ≥70 kg). Although individuals with lower body weight appeared to have slightly higher frequencies of the 5/5 genotype and absence of the 6/6 variant compared to those with higher weight, these differences did not reach statistical significance.

Nevertheless, dopamine plays a well-documented role in mesolimbic dopamine pathway regulation, feeding behaviour, and energy balance [37]. Previous studies have suggested that certain dopamine receptor gene polymorphisms may influence susceptibility to obesity through modulation of food Mesolimbic dopamine pathways [38]. However, our findings do not provide supporting evidence for such an association in current samples.

Table 3: Chi square analysis of Association between Weight and dopamine transporter (SLC6A3) Polymorphisms

	Value	df	Asymp. Sig. (2-sided)	Monte Carlo Sig. (2-sided)		
				Sig.	95% Confidence Interval	
					Lower Bound	Upper Bound
Pearson Chi-Square	1.965[a]	3	0.58	0.57[b]	0.43	0.722
Likelihood Ratio	2.498	3	0.47	0.57[b]	0.43	0.722
Fisher's Exact Test	1.788			0.68[b]	.055	0.824
N of Valid Cases	45					

a. 6 cells (75.0%) have expected count less than 5. The minimum expected count is .67.
b. Based on 45 sampled tables with starting seed 112562564.

It is possible that the relationship between dopamine variants and obesity is influenced by other factors such as dietary habits, lifestyle, or coexisting genetic polymorphisms [39], which were not assessed in this study.

3.4 Association between Age and Interferon gamma Polymorphisms

The distribution of interferon gene variants across age groups is presented in table 4 & figure 4. Among participants younger than 40 years (n = 26), the most common genotype was a/t (38.5%), followed by a/a (23.1%), and equal frequencies of t/t and the null (19.2% each). In participants aged ≥40 years (n = 19), equal frequencies of t/t and a/t genotypes (36.8%), followed by the null (21.1%), while the a/a genotype was relatively rare (5.3%).

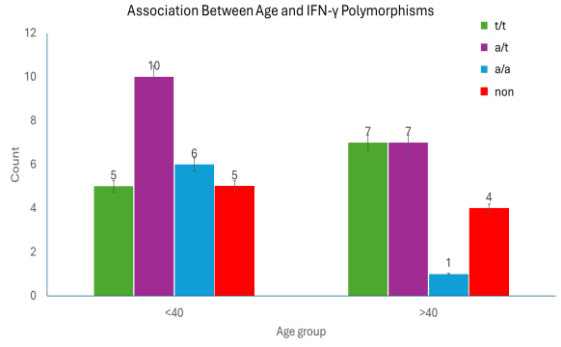

Figure 4. Association between Age and Interferon gamma polymorphisms

Chi-square analysis (table 4) revealed no statistically significant association between age categories and interferon gene variants (p = 0.356).

Table 4: Chi square analysis of Association between Age and Interferon Gamma polymorphisms

	Value	df	Asymp. Sig. (2-sided)	Monte Carlo Sig. (2-sided)		
				Sig.	95% Confidence Interval	
					Lower Bound	Upper Bound
Pearson Chi-Square	3.542[a]	3	.315	.356[b]	.216	.495
Likelihood Ratio	3.848	3	.278	.311[b]	.176	.446
Fisher's Exact Test	3.444			.356[b]	.216	.495
N of Valid Cases	45					

a. 3 cells (37.5%) have expected count less than 5. The minimum expected count is 2.96.
b. Based on 45 sampled tables with starting seed 92208573.

These data suggest that interferon gene variants are not significantly associated with age in this study. Younger members (<40 years) showed a higher proportion of the a/a genotype, whereas older members (≥40 years) demonstrated a greater frequency of the t/t genotype. Despite these observable trends, statistical analysis did not confirm a meaningful age-dependent difference.

The lack of association may reflect the modest sample size and uneven distribution of genotypes, especially the a/a variant in the older group, which reduced the ability to detect significant differences. Interferon-related polymorphisms are known to influence immune responses, inflammation, and susceptibility to infection and malignancies. Age itself is an important determinant of immune function, with younger individuals generally displaying more robust interferon-mediated antiviral responses compared to older adults. However, our data did not support a clear age-related genetic predisposition within the studied group.

Previous studies have suggested that certain interferon gene variants may modulate risk for chronic inflammatory conditions, viral persistence, and even cancer [40]. Since aging is associated with immunosenescence and increased cancer risk [41], for instance Naive T/B cells and DCs in intestinal lymphoid tissue decrease in number with aging, causing gastrointestinal cancers in the elderly [42]. NK T cells show higher cytotoxicity and IFN γ production in centenarians, which is beneficial to fighting diseases and successful aging [43]. Therefore, potential interaction between age and interfere with variants remains biologically plausible.

3.6 Association between Cancer History and Interferon gamma Polymorphisms

The relationship between interferon gene variants and cancer history is shown in table 5 & figure 5. Among participants without a cancer history (n = 28), the distribution of genotypes was relatively balanced: t/t genotype is similar to the null (25.0%). While a/t (28.6%) and a/a (21.4%). In contrast, participants with a cancer history (n = 17) showed a predominance of the a/t genotype (52.9%), followed by t/t (29.4%), while a/a (5.9%) was less frequent.

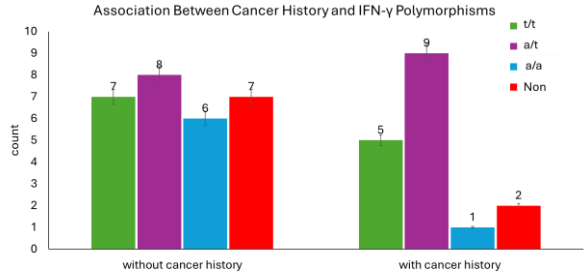

Figure 5. Association between Cancer History and Interferon gamma polymorphisms

Chi-square analysis (Table 5) did not reveal a statistically significant association between cancer history and interferon variants (p = 0.244). The lack of significance may be partly explained by the small subgroup sizes.
Although no statistically significant association was detected, notable trends emerged between interferon variants and cancer history. Individuals with a cancer history were more likely to carry the a/t genotype (52.9%), compared with cancer-free individuals, who displayed a more balanced distribution across all genotypes.

Table 5: Chi square analysis of Association between Cancer History and Interferon Gamma polymorphisms

	Value	df	Asymp. Sig. (2-sided)	Monte Carlo Sig. (2-sided)		
				Sig.	95% Confidence Interval	
					Lower Bound	Upper Bound
Pearson Chi-Square	4.310[a]	3	.230	.222[b]	.101	.344
Likelihood Ratio	4.582	3	.205	.200[b]	.083	.317
Fisher's Exact Test	4.028			.244[b]	.119	.370
N of Valid Cases	45					

a. 4 cells (50.0%) have expected count less than 5. The minimum expected count is 2.64.
b. Based on 45 sampled tables with starting seed 1535910591.

Interferon gene variants are of particular interest because of their established role in regulating immune

responses, antiviral defense, and tumor surveillance [44,45]. The a/t heterozygous state may represent a genotype with differential regulatory activity that could contribute to immune modulation in cancer-prone individuals. Although the present findings did not achieve statistical significance, the skewed distribution of variants—particularly the enrichment of a/t among cancer patients—suggests a possible biological link worth investigating in larger cohorts.

These results align with prior reports linking interferon pathway polymorphisms to altered cytokine expression and immune dysregulation [46], which may facilitate chronic inflammation and carcinogenesis [47]. However, the absence of statistical significance in our study likely reflects both the small sample size and the uneven distribution of genotypes.

4.6 Association between Weight and Interferon gamma Polymorphisms

The relationship between interferon gene variants and weight categories is presented in table 6 & figure 6. Among participants with body weight <70 kg (n = 10), the genotype distribution was t/t (20.0%), a/t (40.0%), a/a (30.0%), and wild type (10.0%). By contrast, individuals with weight ≥70 kg (n = 35) showed a different distribution, with a predominance of the a/t genotype (37.1%), followed by t/t wild (28.6%), null (22.9%), and a/a (11.4%).

Across the entire cohort (n = 45), the most frequent genotype was a/t (37.8%), followed by t/t (26.7%), wild type (20.0%), and a/a mutant (15.6%).

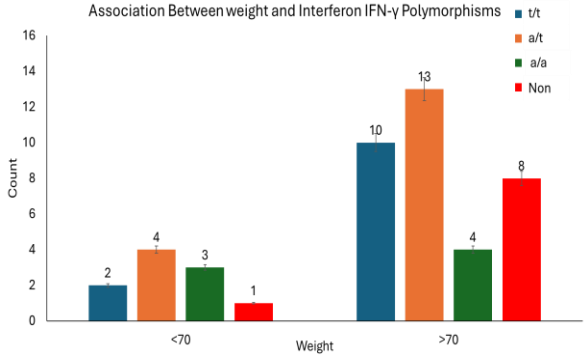

Figure 6. Association between Weight and Interferon gamma polymorphisms

Chi-square analysis (Table 6) did not demonstrate a statistically significant association between interferon variants and weight category (p = 0.578). The validity of the analysis was limited by small subgroup sizes.

Although the association between interferon variants and weight status was not statistically significant, certain trends emerged. Participants with lower body weight (<70 kg) exhibited a relatively higher proportion of the a/a genotype (30.0%) compared with those in the ≥70 kg category (11.4%). Conversely, heterozygous a/t genotypes were more common among heavy weight participants (37.1%). The a/t heterozygous genotype remained the most frequent across both weight categories.

Table 6: Chi square analysis of Association between Weight and Interferon Gamma polymorphisms

	Value	df	Asymp. Sig. (2-sided)	Monte Carlo Sig. (2-sided)		
				Sig.	95% Confidence Interval	
					Lower Bound	Upper Bound
Pearson Chi-Square	2.598[a]	3	.458	.578[b]	.433	.722
Likelihood Ratio	2.470	3	.481	.578[b]	.433	.722
Fisher's Exact Test	2.430			.578[b]	.433	.722
N of Valid Cases	45					

a. 4 cells (50.0%) have expected count less than 5. The minimum expected count is 1.56.
b. Based on 45 sampled tables with starting seed 562334227.

These findings may suggest potential interactions between interferon polymorphisms and weight regulation, although the small subgroup sizes in this study preclude firm conclusions. Interferon-**γ,** encoded by this gene, plays a central role in immune activation and inflammation, processes that are increasingly recognized as contributors to obesity and related metabolic disturbances [48]. Alterations in interferon signalling could therefore influence body weight indirectly through inflammatory pathways or immune-endocrine interactions.

4 Conclusion

This study explored the distribution of dopamine transporter (DAT1 intron 8 VNTR) and interferon-γ (+874 T/A) polymorphisms in relation to age, weight, and cancer history among a cohort of 45 individuals. The findings revealed that while no statistically significant associations were detected, notable patterns emerged. For the DAT1 polymorphism, the 5/6 heterozygous variant was the most common across all age and weight groups, whereas homozygous 6/6 and 5/5 variants appeared less frequently. Similarly, for the interferon-γ polymorphism, the heterozygous a/t genotype was predominant, particularly among individuals with a history of cancer, suggesting a possible biological relevance.

The lack of statistical significance was likely due to the small sample size and low expected frequencies in

some genotype categories.

Taken together, the results emphasize the importance of investigating these genetic variants in larger, more diverse populations. Such efforts may help clarify whether these polymorphisms could serve as biomarkers for disease susceptibility or therapeutic response.

5 Limitation of the Study

The sample size limited the detection of subtle genotype–phenotype associations. Future studies with larger number of volunteers and incorporation of environmental and behavioral data are warranted to clarify whether dopamine variants contribute to obesity risk.

6 Reference

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