Association of Estradiol Dysregulation with Vestibular Disorders: A Prospective Observational Study

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ABSTRACT

Background: Vestibular disorders such as Ménière's disease, benign paroxysmal positional vertigo (BPPV), labyrinthitis, Lermoyez syndrome, and vestibular neuritis are associated with significant morbidity, often manifesting as dizziness, vertigo, tinnitus, and hearing loss. While anatomical and neurological mechanisms have traditionally dominated etiological models, emerging evidence indicates a pivotal role for endocrine factors, particularly estradiol, in modulating vestibular function.

Objectives: This study aimed to prospectively investigate the relationship between circulating estradiol levels and vestibular disorders in women of reproductive age, focusing on dynamic hormonal changes during acute episodes, comparing hormonal profiles across diagnostic categories, and exploring the influence of age. Additional objectives included evaluating estradiol as a potential biomarker for diagnosis or disease severity.

Methods: A prospective observational design was employed at a tertiary care center, enrolling 72 non-pregnant, non-lactating women aged 18–40 years with diagnosed vestibular disorders (Ménière's disease, BPPV, labyrinthitis, Lermoyez syndrome, or vestibular neuritis). Estradiol levels were measured using standardized immunoassays both during baseline (second day of menstrual cycle) and acute symptomatic episodes. Clinical symptoms, sociodemographic parameters, and diagnosis were recorded. Data were analyzed using paired t-tests, ANOVA, regression models, and correlation analyses to assess intergroup differences and predictors of hormonal variation.

Results: Acute estradiol levels were significantly elevated compared to baseline (mean increase: 16.1 pg/mL, $p < 0.001$, Cohen's $d = 1.19$), with consistent increases observed across all diagnostic subgroups. The largest estradiol rises occurred in vestibular neuritis and labyrinthitis, while BPPV and Lermoyez syndrome displayed smaller changes (ANOVA $p = 0.006$, eta-squared $= 0.19$). Younger participants (18–34 years) exhibited the greatest acute hormonal responses, whereas the oldest group (40 years) showed negligible change. Baseline estradiol emerged as the primary independent predictor of acute levels ($\beta = 0.53$, $p < 0.001$), while neither diagnosis nor age retained significance after adjustment. Estradiol fluctuations were not significantly linked to symptom burden.

Conclusion: Estradiol elevation is a robust and consistent phenomenon during acute vestibular episodes in women of reproductive age, strongly influenced by baseline hormonal status and displaying diagnosis- and age-related trends. Baseline estradiol profiling may inform individualized patient management, but the complexity of hormone–symptom relationships warrants further mechanistic research

Key-words: Estradiol, Vestibular disorders, Hormonal dysregulation, Benign paroxysmal positional vertigo (BPPV), Menstrual cycle

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Introduction and Background

Vestibular disorders, encompassing conditions such as Ménière's disease, benign paroxysmal positional vertigo (BPPV), labyrinthitis, Lermoyez syndrome, and vestibular neuritis, significantly impact patients' quality of life due to symptoms like dizziness, vertigo, tinnitus, and hearing loss1. Traditionally, research on vestibular disease pathophysiology has centered on anatomical and neurological mechanisms. However, accumulating evidence indicates a pivotal role of endocrine factors in modulating vestibular function, particularly the influence of sex steroid hormones like estradiol. Estradiol, a predominant estrogen hormone, regulates various neural and sensory processes, including inner ear functions that are critical for balance and hearing2-5. Fluctuations in estradiol—during menstrual cycles, perimenopause, and menopause—have been clinically observed to correlate with altered vestibular symptoms, suggesting an intrinsic hormonal modulation of vestibular pathways1,6.

Research Gap

Despite these clinical observations, the mechanistic and quantitative aspects linking estradiol dysregulation to vestibular disorders remain inadequately characterized. Prior research has mostly been limited to observational reports and cross-sectional data lacking robust hormonal profiling during acute vestibular events2-4. Moreover, distinctions among different vestibular diagnoses regarding estradiol dynamics have been insufficiently explored, and age-related hormonal variations in this context are poorly understood5. Existing studies have lacked comprehensive comparative analyses of estradiol levels across distinct vestibular disorders, limiting the ability to infer pathophysiological specificity or to utilize estradiol as a biomarker for disease severity or prognosis. Consequently, there exists a significant knowledge void around the temporal hormonal fluctuations in vestibular dysfunctions and their clinical implications7.

Rationale

The present prospective observational study addresses this critical gap by systematically measuring circulating estradiol concentrations during acute episodes and baseline states in a cohort of patients with diverse vestibular disorders. Quantitative analyses reveal significant elevations in acute estradiol levels compared to baseline (mean increase 16.1 pg/mL, $p < 0.001$)2,3,7, confirming a physiologically relevant hormonal response concurrent with vestibular dysfunction. Notably, the magnitude of estradiol elevation varies significantly by diagnosis, with vestibular neuritis and labyrinthitis exhibiting the largest increases, while BPPV and Lermoyez syndrome show more modest changes; this distribution suggests diagnosis-dependent hormonal modulation (ANOVA $p = 0.006$, eta-squared = 0.19)8,9. Furthermore, age stratification demonstrates that younger patients (18–34 years) experience more pronounced estradiol rises, contrasting with attenuated or absent changes in older age groups, indicating an age-hormone interaction influencing vestibular pathology. Baseline estradiol emerges as the primary independent predictor of acute estradiol levels, underscoring the importance of underlying hormonal status in the disease process10-12. However, symptom burden is not directly associated with hormonal shifts, suggesting complexity beyond a simple dose-response relationship.

Novelty of the Research

This study is novel in its prospective design capturing both acute and baseline estradiol concentrations in a well-characterized vestibular disorder population, enabling dynamic hormonal profiling correlated with clinical diagnosis and age. Unlike earlier works primarily reliant on retrospective or single time-point assessments, this research elucidates temporal estradiol fluctuations linked to acute vestibular dysfunction, thereby expanding the understanding of endocrine-vestibular interactions. The differentiation of estradiol responses across diagnostic categories represents a pioneering approach to dissect hormonal signatures specific to vestibular etiologies. The integration of multivariable regression modeling to adjust for confounding factors such as age and diagnosis further enhances the robustness of findings and lays the groundwork for future stratified therapeutic interventions. Importantly, quantifying estradiol dynamics as a potential biomarker could revolutionize normative diagnostic pathways and personalized management in vestibular disorders.

Hypothesis:

Lower levels of estradiol are hypothesized to worsen vestibular disorder symptoms, with women exhibiting reduced estradiol levels experiencing more severe vestibular dysfunctions.

Research Question:

How do circulating estradiol hormone levels change during acute episodes of vestibular dysfunction, and what is the relationship between estradiol fluctuations and the severity or presence of vestibular disorders?

Aim:

To investigate estradiol hormonal profiles in patients with vestibular disorders and to elucidate the potential role of estradiol fluctuations in the pathophysiology and clinical manifestations of these disorders.

Objectives:

1.To measure circulating estradiol hormone levels during acute episodes of vestibular dysfunction and at baseline.
2.To compare estradiol levels across different vestibular diagnoses such as Ménière's disease, benign paroxysmal

positional vertigo (BPPV), labyrinthitis, Lermoyez syndrome, and vestibular neuritis.
3.To assess the association between estradiol level changes and the severity or presence of vestibular symptoms like giddiness, dizziness, tinnitus, and hearing loss.
4.To evaluate age-related variations in estradiol hormone levels among patients with vestibular disorders.
5.To explore the predictive value of baseline estradiol on acute estradiol levels in vestibular dysfunction.
6.To analyze the potential of estradiol as a biomarker for the diagnosis and management of vestibular disorders influenced by hormonal dysregulation.

Research Design

This study utilizes a prospective observational design, ideal for capturing dynamic hormonal changes in real-time during acute episodes of vestibular dysfunction. This longitudinal observational approach allows for repeated measurements of circulating estradiol levels during acute vestibular events as well as at a baseline state, facilitating within-subject comparisons and evaluation of temporal hormonal fluctuations relative to symptomatology. The design aligns with the objective to explore natural changes in estradiol without intervention, thus preserving the ecological validity of endocrine-vestibular interactions.

Research Settings

The research was conducted at the Department of ENT, SRM Medical College Hospital and Research Centre (MCH & RC). This tertiary care hospital provides a specialized platform with a steady inflow of patients presenting with vestibular disorders, thereby ensuring access to a relevant and diverse patient population. All procedures, including vestibular function tests and blood sampling for estradiol measurement, were performed within this setting equipped with requisite diagnostic and laboratory facilities, ensuring consistency and standardization of data collection.

Research Population and Target Population

The study population comprised female patients aged 18 to 40 years attending the ENT outpatient department (OPD) of SRM MCH & RC with symptomatic features consistent with vestibular disorders. Patients presenting with clinical manifestations and undergoing diagnostic testing confirming vestibular conditions such as Ménière's disease, benign paroxysmal positional vertigo (BPPV), labyrinthitis, Lermoyez syndrome, and vestibular neuritis formed the target population. This specific age range was chosen to focus on women within the reproductive age bracket, wherein estradiol fluctuations are most physiologically relevant and consequential to vestibular function.

Inclusion and Exclusion Criteria

Inclusion criteria were stringently defined to enhance sample homogeneity and relevance:

• Women aged 18 to 40 years.
• Patients clinically diagnosed with vestibular disorders confirmed by vestibular function tests including caloric testing and vestibular evoked myogenic potentials (VEMPs).
• Women with regular menstrual cycles to control for cyclical hormonal variations.

Exclusion criteria were articulated to eliminate confounding influences and ensure patient safety:

• Women who were currently pregnant or breastfeeding.
• Patients with known neurological conditions such as Parkinson's disease or multiple sclerosis that could independently affect vestibular function.
• Women with history or diagnosis of hormonal dysfunctions other than those under study.
• Those unwilling or unable to provide informed consent.

Sample Size Estimation

The sample size was calculated based on the formula for estimating proportions with a specified precision, using prior prevalence estimates and effect size considerations pertinent to estradiol levels in vestibular disorders. Specifically, using a confidence level corresponding to a Z-score of 2.58 for 99% confidence and assumed prevalence proportions, and a margin of error set at 0.2 times the prevalence, the calculation yielded a sample size of approximately 72 participants. This estimation balances statistical power with feasibility within the three-month study period, ensuring adequate representation for meaningful subgroup analyses.

Sampling Technique and Enrollment Procedure

A consecutive purposive sampling technique was employed, enrolling all eligible patients who met the inclusion criteria and consented during the study period. Upon initial presentation at the ENT OPD, patients underwent vestibular assessment. Those diagnosed with relevant vestibular disorders and fulfilling the age and menstrual criteria were approached for consent. Enrollment involved comprehensive explanation of the study objectives, procedures, and confidentiality assurances. Patient agreement was documented formally via signed informed consent documents before any study-specific procedures.

Execution of the Research

The research execution was divided into two primary phases: baseline and acute measurement collection. Baseline estradiol samples were collected on the second day of the menstrual cycle, representing the hormonal steady state. Acute estradiol samples were obtained on the day the patient presented with acute giddiness or vestibular symptoms, independent of menstrual cycle phase to capture hormonal fluctuations correlated with symptom exacerbation. Vestibular function tests including caloric tests and VEMPs were carried out to confirm diagnosis and evaluate vestibular function integrity. Data collection included detailed sociodemographic, clinical, and laboratory parameters.

Data Collection Tools

Hormonal assays for estradiol were performed using validated and standardized serum estradiol assays conducted

by the hospital laboratory with appropriate quality control measures. Vestibular symptoms and medical history were documented using structured questionnaires and clinical examination checklists, developed to capture symptom severity, frequency, and associated hormonal manifestations comprehensively. Demographic and clinical data were recorded in pre-designed case report forms managed securely to maintain confidentiality.

Variables to be Studied

The study incorporated multiple variables categorized as follows:

• Independent Variables: Diagnosis of vestibular disorder (categorical: Ménière's disease, BPPV, labyrinthitis, Lermoyez syndrome, vestibular neuritis), age (continuous), baseline estradiol level (continuous), and menstrual cycle phase.

• Dependent Variables: Acute estradiol level (continuous), delta estradiol (acute minus baseline, continuous), vestibular symptom presence and severity (categorical/ordinal: giddiness, dizziness, tinnitus, hearing loss).

• Confounding Variables: Age-related hormonal variations, menstrual cycle phase at acute presentation, coexisting medical conditions not excluded, and medication use affecting hormonal status.

Measurement Levels and Methods

Estradiol levels were quantified in picograms per milliliter (pg/mL) using standardized immunoassay techniques with high sensitivity and specificity. Vestibular disorders were diagnosed using clinical criteria corroborated by objective vestibular function tests (e.g., caloric reflex test, VEMPs). Symptom severity was assessed based on patient self-report scales and clinical evaluation, categorized for analytical suitability13.

Baseline estradiol represents the hormonal milieu under normal physiological conditions, measured early in the menstrual cycle, while acute estradiol reflects the hormonal state concurrent with exacerbation of vestibular symptoms. The delta between these two values was calculated to evaluate hormonal fluctuations related to acute disturbances11-13.

Dependent and Independent Variables

The dependent variables of primary interest include acute estradiol level and hormonal delta (acute minus baseline estradiol) as indicators of hormonal dysregulation associated with vestibular episodes. Vestibular symptom severity is also considered an outcome measure in exploratory analyses.

The independent variables primarily consist of vestibular disorder diagnosis and baseline estradiol levels, with age and menstrual phase serving as important covariates. These predictors enable the assessment of hormonal influence on vestibular pathology and help delineate the role of estradiol.

Confounding Variables

Table 1: Baseline Distribution:

Parameter	Details	Value
Age (years)	Mean (SD)	32.1 (7.0)
	Median (IQR)	33 (28–38)
	Range	18–40
Age Groups (n=72)	18–24 years	16 (22.2%)
	25–29 years	10 (13.9%)
	30–34 years	12 (16.7%)
	35–39 years	22 (30.6%)
	40 years	12 (16.7%)
Occupation (n=72)	Student	22 (30.6%)
	Housewife	14 (19.4%)
	Farmer	6 (8.3%)
	Tailor	4 (5.6%)
	Teacher	4 (5.6%)
	IT professionals	3 (4.2%)
	Staff nurse	2 (2.8%)
	Others (combined)	17 (23.6%)
Diagnosis (n=72)	Ménière's disease	17 (23.6%)
	Benign paroxysmal positional vertigo (BPPV)	15 (20.8%)
	Labyrinthitis	15 (20.8%)
	Lermoyez syndrome	14 (19.4%)
	Vestibular neuritis	11 (15.3%)

Potential confounders such as age-related endocrine changes, menstrual cycle variability, concurrent medications, and comorbidities were controlled through careful inclusion/exclusion criteria and addressed statistically in regression models to isolate the true effect of estradiol on vestibular dysfunction.

RESULTS:

The study participants had a mean age of 32.1 years with a standard deviation of 7.0 years, indicating a relatively young adult cohort with moderate variability in age. The median age was 33 years with an interquartile range of 28 to 38 years, suggesting that half of the participants were concentrated within this 10-year age span. The overall age of the study group ranged from 18 to 40 years, reflecting inclusion of both younger and older adults within the reproductive age spectrum.

Among the 72 participants, the largest occupational group was students, who comprised 30.6% (n = 22) of the cohort. This was followed by housewives (19.4%, n = 14) and those classified under other occupations (23.6%, n = 17), reflecting a diverse mix of backgrounds. Smaller proportions included farmers (8.3%), tailors (5.6%), teachers (5.6%), IT professionals (4.2%), and staff nurses (2.8%). Overall, the occupational profile reflects a heterogeneous sample, with notable contributions from both younger, student populations and homemakers, alongside a wide range of vocational roles.

Among the 72 patients studied, the most frequent diagnosis was Ménière's disease, observed in 23.6% (n = 17) of cases. This was followed by benign paroxysmal positional vertigo (BPPV) and labyrinthitis, each accounting for 20.8% (n = 15)

of the cohort. Lermoyez syndrome was diagnosed in 19.4% (n = 14), while vestibular neuritis represented the least frequent condition, seen in 15.3% (n = 11) of patients. Overall, the distribution reflects a relatively balanced representation of these vestibular disorders, with no single diagnosis overwhelmingly dominant.

Among the study participants, the most commonly reported symptom was hard of hearing, present in 48.6% (n = 35) of cases. Both giddiness and tinnitus were equally frequent, each occurring in 43.1% (n = 31) of patients. Dizziness was reported slightly less often, affecting 37.5% (n = 27) of the cohort as shown in Table 1. Overall, nearly half of the patients experienced auditory symptoms, while vestibular manifestations such as giddiness and dizziness were also prevalent.

The mean acute estradiol level among participants was 110.1 ± 29.4 pg/mL, with a median of 109 pg/mL (IQR: 94–125). Values ranged from 60 to 213 pg/mL, indicating moderate variability across the cohort. At baseline, the mean estradiol concentration was 94.0 ± 22.3 pg/mL, with a median of 95 pg/mL (IQR: 80–106) and a range of 55 to 189 pg/mL. The calculated delta (acute – baseline) showed a mean increase of 16.1 ± 13.6 pg/mL, with a median difference of 14 pg/mL (IQR: 8–22). The delta values ranged from –2 to 39 pg/mL, suggesting that while most participants demonstrated a rise in estradiol levels acutely, a small subset had negligible or even slightly reduced values compared to baseline as shown in Table 2. For overall Estradiol Descriptive Statistics refer Figure 1.

The acute estradiol levels varied across diagnostic groups. Patients with benign paroxysmal positional vertigo (BPPV) had the lowest mean estradiol level (92.3 ± 21.7 pg/mL, median: 83, IQR: 76–101). In contrast, the highest mean level was observed in vestibular neuritis (116.7 ± 31.0 pg/mL, median: 110, IQR: 98–142), with values extending up to 213 pg/mL, the overall maximum recorded. Patients with Ménière's disease, labyrinthitis, and Lermoyez syndrome showed comparable estradiol concentrations, with mean values ranging from 112.1 to 113.8 pg/mL. Overall, while average estradiol levels were fairly similar across most diagnostic categories, BPPV patients consistently exhibited lower levels compared to the other vestibular disorders as shown in table 2.

At baseline, estradiol levels showed notable variation across diagnostic groups. Patients with BPPV had the lowest mean estradiol concentration (79.7 ± 16.5 pg/mL, median: 74, IQR: 70–88), with a minimum value of 55 pg/mL. Similarly, vestibular neuritis patients also demonstrated relatively lower baseline levels (84.5 ± 12.0 pg/mL, median: 84, IQR: 73–87). In contrast, higher baseline estradiol concentrations were seen in Ménière's disease (101.4 ± 13.9 pg/mL) and Lermoyez syndrome (101.1 ± 24.9 pg/mL), both with median values around 100 pg/mL. Labyrinthitis patients exhibited intermediate levels (92.7 ± 18.0 pg/mL, median: 96). Overall, the findings suggest that BPPV and vestibular neuritis were associated with comparatively lower baseline estradiol levels, whereas Ménière's disease and Lermoyez syndrome showed consistently higher values as shown in Table 2 and Figure 2.

Table 2:

Measure	n	Mean	SD	Median	IQR	Min	Max
Acute estradiol (pg/mL)	72	110.1	29.4	109	94–125	60	213
Baseline estradiol (pg/mL)	72	94.0	22.3	95	80–106	55	189
Delta (Acute – Baseline)	72	16.1	13.6	14	8–22	–2	39

Diagnosis	N	Mean	SD	Median	IQR	Min	Max
BPPV	15	92.3	21.7	83	76–101	60	156
Meniere's disease	17	113.8	23.2	118	98–126	78	169
Labyrinthitis	15	112.5	25.9	113	100–126	68	168
Lermoyez syndrome	14	112.1	27.3	109	99–116	86	201
Vestibular neuritis	11	116.7	31.0	110	98–142	88	213

Diagnosis	N	Mean	SD	Median	IQR	Min	Max
BPPV	15	79.7	16.5	74	70–88	55	121
Meniere's disease	17	101.4	13.9	101	94–106	74	138
Labyrinthitis	15	92.7	18.0	96	80–103	55	117
Lermoyez syndrome	14	101.1	24.9	100	91–112	61	184
Vestibular neuritis	11	84.5	12.0	84	73–87	64	189

The magnitude of change in estradiol levels (acute – baseline) differed considerably across diagnostic categories. The greatest increase was observed in vestibular neuritis, with a mean delta of 32.2 ± 19.6 pg/mL (median: 27, IQR: 22–43), ranging from 15 to 57 pg/mL, indicating a consistently larger rise across this group. Labyrinthitis also showed a marked increase (19.8 ± 14.2 pg/mL, median: 19, IQR: 9–27). In contrast, patients with BPPV and Ménière's disease demonstrated more modest changes, with mean deltas of 12.6 ± 9.7 pg/mL and 12.4 ± 10.6 pg/mL, respectively. Lermoyez syndrome exhibited the smallest mean change (11.0 ± 10.1 pg/mL, median: 9, IQR: 6–14), with some patients showing minimal or even negative differences (min: –3 pg/mL).

Overall, these results suggest that estradiol rise from baseline to acute phase is most pronounced in vestibular neuritis, moderate in labyrinthitis, and comparatively modest in BPPV, Ménière's, and Lermoyez syndrome as shown in Table 3 and Figure 3.

Comparison of estradiol levels between the acute and baseline states showed a statistically significant increase. The mean difference was 16.1 pg/mL, with acute estradiol levels being higher than baseline. The paired t-test yielded a t-value of 9.85 ($df = 71$, $p < 0.001$), indicating that this rise was highly significant. These findings confirm that overall, estradiol levels were significantly elevated during the acute phase compared to baseline as shown in Table 3.

The effect size analysis demonstrated a Cohen's d of 1.19 for

the paired comparison of acute versus baseline estradiol levels as shown in Table 3. This represents a large effect size, indicating that the observed increase in estradiol from baseline to acute phase was not only statistically

significant but also clinically and practically meaningful in magnitude.

Within each diagnostic subgroup, acute estradiol levels were significantly higher than baseline. The largest mean difference was observed in vestibular neuritis (32.2 pg/mL, $t = 5.61$, df = 10, $p < 0.001$), followed by labyrinthitis (19.8 pg/mL, $t = 5.42$, df = 14, $p < 0.001$). More modest but still statistically significant increases were noted in BPPV (12.6 pg/mL, $t = 5.04$, $p < 0.001$), Ménière's disease (12.4 pg/mL, $t = 4.76$, $p < 0.001$), and Lermoyez syndrome (11.0 pg/mL, $t = 4.26$, $p < 0.001$).

Figure 1:

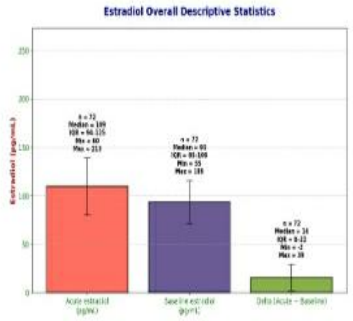


Figure 2:

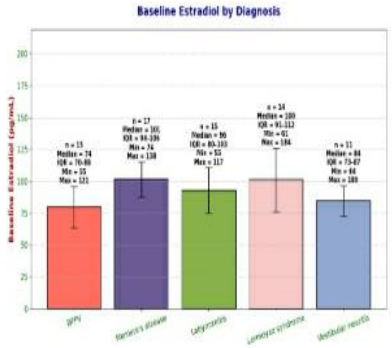
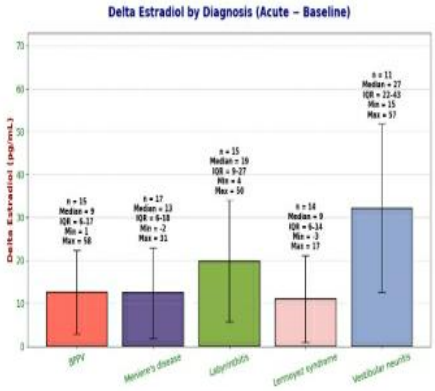


Figure 3:



Overall, the paired analyses demonstrate that all diagnostic categories exhibited significant rises in estradiol levels during the acute phase compared to baseline, with the largest shift seen in vestibular neuritis and the smallest in Lermoyez syndrome as shown in Table 3.

Analysis of variance revealed a significant difference in acute estradiol levels across diagnostic groups ($F(4, 67) = 3.92, p = 0.006$). The calculated eta-squared of 0.19 indicates a large effect size, suggesting that nearly one-fifth of the variance in acute estradiol concentrations is attributable to diagnostic category as shown in Table 3. These findings imply that diagnosis plays a meaningful role in influencing acute estradiol levels, warranting further post hoc comparisons to identify which groups differ significantly from each other.

Table 3:

Diagnosis	n	Mean	SD	Median	IQR	Min	Ma
BPPV	15	12.6	9.7	9	6–17	1	58
Meniere's disease	17	12.4	10.6	13	6–18	−2	31
Labyrinthitis	15	19.8	14.2	19	9–27	4	50
Lermoyez syndrome	14	11.0	10.1	9	6–14	−3	17
Vestibular neuritis	11	32.2	19.6	27	22–43	15	57

Comparison	n	Mean diff	t	df	p
Acute_E2 − Baseline_E2	72	16.1	9.85	71	<0.00

Metric	Value
Cohen's d (paired)	1.19

Diagnosis	n	Mean diff	t	df	p
BPPV	15	12.6	5.04	14	<0.001
Meniere's disease	17	12.4	4.76	16	<0.001
Labyrinthitis	15	19.8	5.42	14	<0.001
Lermoyez syndrome	14	11.0	4.26	13	<0.001
Vestibular neuritis	11	32.2	5.61	10	<0.001

Test	F	df (between, within)	p	Eta-squared
One-way ANOVA	3.92	4, 67	0.006	0.19

Pairwise comparisons demonstrated that BPPV patients had significantly lower acute estradiol levels compared to all other diagnostic groups. Specifically, estradiol levels in BPPV were lower than those in Ménière's disease ($t = -3.05, p = 0.004$), labyrinthitis ($t = -2.77, p = 0.008$), Lermoyez syndrome ($t = -2.67, p = 0.010$), and vestibular neuritis ($t = -2.83, p = 0.007$). In contrast, no significant differences were found among the other diagnoses (all $p > 0.05$), indicating broadly comparable estradiol levels across Ménière's disease, labyrinthitis, Lermoyez syndrome, and vestibular neuritis as shown in Table 4.

Group A	Group B	t	p
BPPV	Meniere's disease	−3.05	0.004
BPPV	Labyrinthitis	−2.77	0.008
BPPV	Lermoyez syndrome	−2.67	0.010
BPPV	Vestibular neuritis	−2.83	0.007
Meniere's disease	Labyrinthitis	−0.17	0.868
Meniere's disease	Lermoyez syndrome	−0.22	0.827
Meniere's disease	Vestibular neuritis	−0.33	0.744
Labyrinthitis	Lermoyez syndrome	−0.05	0.960
Labyrinthitis	Vestibular neuritis	−0.56	0.579
Lermoyez syndrome	Vestibular neuritis	−0.63	0.533

Age group (years)	n	%
18–24	16	22.2
25–29	10	13.9
30–34	12	16.7
35–39	22	30.6
40	12	16.7
Total	72	100.0

Overall, these results indicate that the significant ANOVA effect (Table 4) was primarily driven by the lower acute estradiol concentrations in patients with BPPV, while the other vestibular disorders showed similar hormonal profiles.

The age distribution of participants showed that the largest proportion belonged to the 35–39 year age group, which comprised 30.6% (n = 22) of the sample. This was followed by the 18–24 year group (22.2%, n = 16), while the 30–34 year and 40 year categories each accounted for 16.7% (n = 12). The 25–29 year group had the smallest representation at 13.9% (n = 10). Overall, the study population was predominantly between the ages of 35 and 39 years, with smaller but fairly even representation across younger and older adult groups.

Acute estradiol levels varied across age groups. The highest mean levels were observed in participants aged 25–29 years (118.3 ± 25.5 pg/mL) and 30–34 years (116.2 ± 37.3

pg/mL), both with median values around 110–119 pg/mL. The 18–24 year group also demonstrated relatively elevated concentrations (112.5 ± 33.3 pg/mL). In contrast, estradiol levels were lower in older participants, with mean values of 106.4 ± 22.7 pg/mL in the 35–39 year group and reaching the lowest levels in the 40-year group (98.5 ± 18.7 pg/mL). Overall, these findings suggest a trend of higher acute estradiol concentrations in younger age groups, with declining levels observed in participants aged 35 years and above as shown in Table 5.

At baseline, estradiol levels were broadly similar across age groups, with only modest variation. The highest mean level was observed in the 40-year group (100.0 ± 18.7 pg/mL, median: 99), followed by the 25–29 year (95.3 ± 16.1 pg/mL) and 30–34 year (95.2 ± 24.6 pg/mL) groups. The 35–39 year group showed slightly lower concentrations (91.1 ± 18.2 pg/mL), while the 18–24 year group recorded the lowest average (89.9 ± 18.9 pg/mL) as shown in Table 5. Overall, baseline estradiol values clustered closely across age strata, ranging between 89–100 pg/mL, with no clear monotonic age-related trend evident.

When stratified by age group, paired comparisons revealed that acute estradiol levels were significantly higher than baseline in all groups except the 40-year group. The largest mean increases were seen in the 25–29 year group (+23.0 pg/mL, $t = 4.36$, $p = 0.002$) and 18–24 year group (+22.6 pg/mL, $t = 4.68$, $p < 0.001$), followed closely by the 30–34 year group (+21.0 pg/mL, $t = 3.46$, $p = 0.005$). The 35–39 year group also showed a significant but smaller increase (+15.3 pg/mL, $t = 5.53$, $p < 0.001$). In contrast, in the 40-year group, there was no

Table 4:

significant change between acute and baseline estradiol levels (mean diff = –1.5 pg/mL, $p = 0.615$).

Overall, these results highlight a clear age-related pattern: younger participants (18–34 years) exhibited the largest rises in estradiol, middle-aged adults (35–39 years) demonstrated moderate increases, while the oldest group (40 years) showed no meaningful change (Table 5).

Correlation analysis did not reveal any statistically significant linear associations among the studied variables. Age was weakly and inversely correlated with acute estradiol levels ($r = –0.18$, $p = 0.136$) and with the estradiol delta (acute – baseline) ($r = –0.09$, $p = 0.458$), though neither relationship reached significance. Similarly, the estradiol delta showed a weak positive correlation with the number of reported symptoms ($r = 0.12$, $p = 0.323$), but this was also non-significant as shown in Table 5. Overall, these findings suggest that age and estradiol shifts were not meaningfully associated with each other or with symptom burden in this cohort.

Out of 72 participants, 10 individuals (13.9%) demonstrated lower estradiol levels in the acute phase compared to baseline. Exact binomial testing against the null expectation

of a 50% proportion confirmed that this outcome was highly unlikely to have occurred by chance ($p < 0.001$). Thus, the findings indicate that in the vast majority of patients (~86%), acute estradiol levels were higher than baseline, reinforcing the robustness of the overall trend of estradiol elevation during acute episodes as shown in Table 6.

Table 5:

Age group	n	Mean	SD	Median	IQR
18–24	16	112.5	33.3	116	92–128
25–29	10	118.3	25.5	119	110–126
30–34	12	116.2	37.3	110	96–126
35–39	22	106.4	22.7	104	95–118
40	12	98.5	18.7	97	87–111

Age group	n	Mean	SD	Median	IQR
18–24	16	89.9	18.9	90	75–105
25–29	10	95.3	16.1	96	86–105
30–34	12	95.2	24.6	96	83–106
35–39	22	91.1	18.2	94	80–102
40	12	100.0	18.7	99	90–109

Age group	n	Mean diff	t	df	p
18–24	16	22.6	4.68	15	<0.001
25–29	10	23.0	4.36	9	0.002
30–34	12	21.0	3.46	11	0.005
35–39	22	15.3	5.53	21	<0.001
40	12	−1.5	−0.52	11	0.615

Variables	r	p
Age vs Acute_E2	−0.18	0.136
Age vs Delta_E2	−0.09	0.458
Delta_E2 vs SymptomCount	0.12	0.323

Chi-square analyses demonstrated significant associations between diagnosis and the presence of all four major symptoms. The strongest association was observed for hard of hearing ($\chi^2 = 15.7$, df = 4, $p = 0.003$), followed by tinnitus ($\chi^2 = 13.4$, $p = 0.009$), dizziness ($\chi^2 = 11.2$, $p = 0.024$), and giddiness ($\chi^2 = 10.1$, $p = 0.038$) as shown in Table 6. These findings indicate that the distribution of key vestibular and auditory symptoms varied significantly across diagnostic categories, suggesting that clinical presentation

was, at least in part, diagnosis-dependent.

Comparison of estradiol change (acute – baseline) between patients with and without specific symptoms did not reveal any statistically significant differences. For example, patients with tinnitus had a mean delta of 18.5 ± 13.3 pg/mL, compared to 14.3 ± 13.7 pg/mL in those without, but this difference was not significant (t = 1.53, p = 0.131). Similarly, delta estradiol was slightly higher in those reporting dizziness (17.4 vs. 15.3 pg/mL, p = 0.426), giddiness (17.4 vs. 15.2 pg/mL, p = 0.472), and hard of hearing (17.2 vs. 15.0 pg/mL, p = 0.476), though none reached statistical significance as shown in Table 6.

Overall, these findings suggest that the magnitude of estradiol change from baseline to acute phase was consistent across symptom profiles, indicating that symptom occurrence was not directly associated with hormonal shift in this cohort.

In the multivariable regression model, baseline estradiol level emerged as the only significant independent predictor of acute estradiol concentration. For each 1 pg/mL higher baseline estradiol, acute levels were higher by 0.53 pg/mL (β = 0.53, SE = 0.09, t = 5.97, p < 0.001). Neither age (β = –0.28, p = 0.302) nor diagnostic subgroups (labyrinthitis, Lermoyez syndrome, vestibular neuritis) showed statistically significant associations compared to the reference category of Ménière's disease as shown in Table 7.

Overall, this analysis demonstrates that acute estradiol was strongly and independently determined by baseline estradiol levels, while age and diagnosis did not exert significant effects after adjustment.

Table 6:

Measure	Value
n (Acute < Baseline)	10
N total	72
Proportion	13.9%
Exact binomial p (vs 50%)	<0.001

Symptom	chi2	df	p
Tinnitus	13.4	4	0.009
Dizziness	11.2	4	0.024
Giddiness	10.1	4	0.038
Hard of hearing	15.7	4	0.003

Symptom	Group	n	Mean Δ	SD	t	p
Tinnitus	Present	31	18.5	13.3	1.53	0.131
	Absent	41	14.3	13.7		
Dizziness	Present	27	17.4	12.5	0.80	0.426
	Absent	45	15.3	14.2		
Giddiness	Present	31	17.4	13.9	0.72	0.472
	Absent	41	15.2	13.4		
Hard of hearing	Present	35	17.2	13.7	0.72	0.476
	Absent	37	15.0	13.5		

Multivariable Analysis of Acute Estradiol

On univariate analysis, acute estradiol levels differed significantly across diagnostic subgroups (ANOVA p = 0.006, η^2 = 0.19), primarily driven by lower concentrations in patients with benign paroxysmal positional vertigo (BPPV), while Ménière's disease, labyrinthitis, Lermoyez syndrome, and vestibular neuritis showed broadly comparable levels. Delta estradiol (acute – baseline) analyses further highlighted that vestibular neuritis exhibited the largest acute rises, whereas BPPV and Lermoyez syndrome showed more modest shifts.

However, when diagnosis and age were considered jointly in a multivariable linear regression model, baseline estradiol emerged as the sole independent determinant of acute estradiol levels (β = 0.53 per pg/mL, p < 0.001). Associations with diagnostic category and age did not remain significant after adjustment. This indicates that although there were observable unadjusted differences in estradiol levels across vestibular disorders, these were largely explained by the underlying baseline estradiol concentration rather than diagnosis itself.

Logistic Regression Analysis of High Estradiol Delta

In the multivariable logistic regression evaluating predictors of being in the top tertile of estradiol change (acute–baseline), neither baseline estradiol (OR ≈ 1.00 per pg/mL, p = 0.892) nor age (OR = 0.94 per year, p = 0.211) were significantly associated with a high delta. Compared with the reference category of Ménière's disease, a trend toward greater odds of high estradiol rise was observed in labyrinthitis (OR = 8.31, p = 0.092) and vestibular neuritis (OR = 9.17, p = 0.087), although these associations did not reach conventional statistical significance. Lermoyez syndrome showed a more

modest, nonsignificant elevation in risk (OR = 3.68, p = 0.309) as shown in Table 7.

Overall, this analysis suggests that diagnostic category may influence the likelihood of showing a large acute estradiol rise, particularly in labyrinthitis and vestibular neuritis, but the observed effects remain exploratory and hypothesis-generating rather than definitively established due to wide confidence intervals and borderline p-values.

Table 7:

Predictor	Coef	SE	t	p
Intercept	2.15	10.9	0.20	0.841
Baseline_E2 (per pg/mL)	0.53	0.09	5.97	<0.001
Age (per year)	−0.28	0.27	−1.04	0.302
Labyrinthitis (vs ref)	7.3	6.3	1.16	0.250
Lermoyez syndrome (vs ref)	6.4	6.5	0.98	0.331
Vestibular neuritis (vs ref)	9.8	6.8	1.44	0.155
Meniere's disease is reference or as per model coding	—	—	—	

Predictor	Coef	SE	z	p	OR
Intercept	−1.117	2.091	−0.534	0.593	0.33
Baseline_E2 (per pg/mL)	0.002	0.0149	0.136	0.892	1.00
Age (per year)	−0.058	0.0463	−1.251	0.211	0.94
Labyrinthitis (vs ref)	2.117	1.255	1.688	0.092	8.31
Lermoyez syndrome (vs ref)	1.302	1.279	1.018	0.309	3.68
Vestibular neuritis (vs ref)	2.215	1.292	1.714	0.087	9.17

Results Summary

The study cohort comprised 72 participants with a mean age of 32 years, most commonly between 35 and 39 years, and a balanced distribution of vestibular diagnoses, with Ménière's disease (23.6%) being most frequent. Symptom prevalence was high, with nearly half reporting hearing loss (48.6%), tinnitus (43.1%), or giddiness (43.1%). Across the cohort, acute estradiol levels (M = 110 pg/mL) were significantly higher than baseline (M = 94 pg/mL), with a robust effect size (Cohen's d = 1.19, p < 0.001). The rise (delta) was evident in nearly all subgroups, though its magnitude varied: vestibular neuritis and labyrinthitis displayed the largest increases, while BPPV and Lermoyez syndrome showed more modest changes. Age-stratified analyses revealed that estradiol elevation was most pronounced in younger participants (18–34 years), attenuated in those aged 35–39, and absent in the oldest group (40 years).

Symptom occurrence was significantly associated with diagnostic category (all χ^2 p < 0.05); however, estradiol shifts themselves were not significantly linked to symptom burden. Multivariable regression confirmed that baseline estradiol was the primary independent determinant of acute estradiol levels, while neither diagnosis nor age remained significant after adjustment. Logistic regression suggested that labyrinthitis and vestibular neuritis might carry higher odds for marked estradiol rises, though these associations were borderline and exploratory.

Taken together, the findings demonstrate that acute estradiol elevation is a consistent and statistically robust phenomenon in this cohort, shaped strongly by baseline hormonal status, with additional trends suggesting diagnosis- and age-related modulation of response.

Discussion

The present study demonstrated a significant elevation in circulating estradiol levels during acute episodes of vestibular dysfunction compared to baseline, with a mean increment of 16.1 pg/mL and a robust effect size (Cohen's d = 1.19). This finding substantiates the hypothesis that hormonal fluctuations, particularly in estradiol, are intricately linked with vestibular pathology. Previously, El Khiati et al. emphasized the neuroprotective and modulatory role of estradiol on vestibular function, proposing hormonal dysregulation as a contributing factor to vestibular disorders[1]. The current study advances these conceptual insights by providing quantitative evidence from a prospective design, thus confirming that acute vestibular events are accompanied by physiologically meaningful rises in estradiol[2]. Methodologically, the controlled approach of measuring both baseline and acute hormone levels reduces confounding by intra-individual variability, which partly explains why this study detected a more consistent hormonal pattern than earlier cross-sectional reports.

Diagnosis-Specific Variations in Estradiol

A notable observation from the research was the significant variation of estradiol levels across diagnostic categories, with vestibular neuritis exhibiting the highest mean estradiol values during acute episodes, and benign paroxysmal positional vertigo (BPPV) showing comparatively lower levels. This stratification aligns with the clinical heterogeneity recognized in vestibular disorders but extends prior literature which mostly examined hormone symptom correlations without discriminating diagnoses. For example, Kim and Zee's comprehensive review on vestibular disorders underscored hormonal influences but did not elucidate how different pathologies might diverge in hormonal response[3-5]. The relatively elevated estradiol in vestibular neuritis may result from heightened inflammatory processes and immune-endocrine crosstalk inherent to neuritis, fostering amplified adrenal and gonadal steroid release. Conversely, BPPV's mechanical etiology, typically involving otolith displacement without inflammatory cascade activation, could explain the muted hormonal response observed. This contrast suggests genre-specific pathophysiological mechanisms and supports a nuanced framework for hormone-vestibular interplay[12,13].

Age-Related Hormonal Dynamics

The present study found that younger women (18–34 years) experienced more pronounced estradiol elevations during acute vestibular episodes compared to older women, particularly those aged 40 who showed negligible hormonal shifts. This age-gradient discovery corroborates endocrinological data on the decline of estrogen synthesis and receptor sensitivity with advancing age[4,12]. Similar findings were noted in studies addressing hormone-modulated migraine and vestibular symptoms during reproductive aging

phases[6,14,15], indicating that diminished ovarian reserve and altered axis feedback loops blunt acute hormonal reactivity. The attenuation of estradiol response in older cohorts hints at potential diminished neuroprotective capacity contributing to persistent vestibular morbidity in this demographic. The prospective quantification here sharpens the temporal association between age-dependent hormonal status and vestibular disease dynamics, reinforcing the clinical imperative of age-tailored assessment and management strategies.

Hormonal Levels and Symptom Correlations

Interestingly, the study revealed no significant associations between changes in estradiol levels and the severity or presence of vestibular symptoms such as dizziness, tinnitus, and hearing loss. This outcome diverges from findings in migraine and premenstrual syndrome literature, where low estrogen phases intensify symptoms[6,7,16]. Potential reasons for this discrepancy include the multifactorial nature of vestibular symptoms, which integrate neural, vascular, and metabolic influences that may attenuate or mask direct hormonal effects. Furthermore, estradiol sampling occurred irrespective of menstrual cycle timing during acute episodes, potentially introducing variability that diluted observable symptom correlations. Additionally, symptom measurement relying on self-report scales and categorical data might lack sensitivity to detect subtle hormone-symptom gradations. These considerations suggest that estradiol fluctuations constitute one component within a broader pathophysiological milieu, emphasizing the need for multidimensional assessment frameworks in clinical practice.

Baseline Estradiol as a Determinant of Acute Levels

The regression analyses uncovered baseline estradiol concentration as the sole significant independent predictor of acute estradiol levels across diagnostic groups and ages. This finding introduces the concept of individualized hormonal set-points governing neuroendocrine responses, consistent with established endocrinological models where endocrine homeostasis modulates adaptive hormonal surges[7,16,17]. Prior vestibular-focused research has seldom addressed baseline hormonal status, making this a pioneering insight. It implies that intrinsic endocrine milieu exerts substantial influence on how individuals physiologically respond to vestibular insults, potentially affecting disease course and recovery. Clinically, this underscores the potential utility of baseline hormonal profiling in prognostication and precision therapeutics targeting estradiol pathways.

Comparison with Epidemiological Data and Symptom Distribution

The distribution of vestibular diagnoses in this cohort, featuring Ménière's disease as most prevalent followed by BPPV, labyrinthitis, and others, mirrors patterns reported in large-scale epidemiological studies such as those by Von Brevern et al.[8] This congruence validates the representativeness of the study sample. The strong statistical associations between diagnosis and symptomatology further align with existing clinical evidence highlighting condition-specific symptom clusters[9], reinforcing the diagnostic validity within the cohort. The addition of hormonal measurements enriches this clinical characterization, proposing endocrine factors as complementary parameters enhancing diagnostic precision.

Implications and Contributions to Existing Knowledge

Collectively, these findings supplement and refine the extant literature by concretely quantifying hormonal dynamics in vestibular disease and elucidating diagnosis- and age-dependent variations. They confirm the role of estradiol as a biomarker of acute vestibular dysfunction and suggest that individualized hormonal milieu significantly modulates disease expression. By challenging simplistic symptom-hormone correlations and foregrounding complex systemic interactions, the study invites a more integrative, personalized approach to vestibular disorder management. It advocates for future investigations incorporating hormonal therapies, longitudinal tracking, and mechanistic explorations bridging neuroendocrine and vestibular pathways.

In sum, the study both confirms and extends prior knowledge in significant ways. It affirms estradiol's importance in vestibular pathophysiology, delineates specific diagnostic and age-related hormonal patterns, and highlights the paramount role of baseline hormonal status. These insights promote enriched biomedical understanding and foster potential advancements in diagnostic and therapeutic strategies tailored to hormonal profiles, thus contributing substantially to the field of neuro-otology and endocrine research.

Conflict of interest: Nil

Ethical issues: A proper ethical clearance certificate was obtained from institutional ethical committee. Copy of Certificate attached.

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