

**Menopausal symptoms, quality of life, postural balance and
cognitive functions in a community based population of Sri
Lankan women**

by
Himansu Waldyasekera



Ph.D

2009

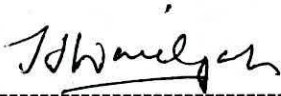
Menopausal symptoms, quality of life, postural balance and
cognitive functions in a community based population of Sri
Lankan women

by

Himansu Waidyasekera

Thesis submitted to the University of Sri Jayewardenepura for
the award of the degree of Doctor of Philosophy in Physiology
on 27th February, 2009

The work described in this thesis was carried out by me under the supervision of Prof. Kumudu Wijewardene of the University of Sri Jayewardenepura, Sri Lanka, Prof. Tord Naessen and Prof. Gunilla Lindmark of the University of Uppsala, Sweden and a report on this has not been submitted in whole or in part to any university or any other institution for another degree / diploma.



Date 26 / 02 / 2009

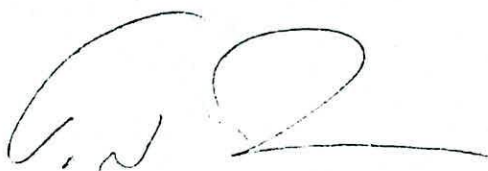
Himansu Waidyasekera
Department of Physiology
Faculty of Medical Sciences
University of Sri Jayewardenepura
Nugegoda, Sri Lanka.

We certify that the above statement made by the candidate is true and that this thesis is suitable for submission to the University for the purpose of evaluation.



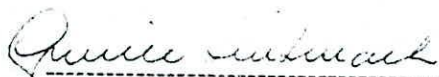
Prof. Kumudu Wijewardene
~~Dean, Faculty of Graduate studies,~~
University of Sri Jaywardenepura

Date 26. 2. 2009



Prof. Tord Naessen,
Department of Women's and Children's Health,
Section for Women's and Children's Health,
University Hospital, Uppsala,
Sweden


Date Feb. 28, 2009



Prof. Gunilla Lindmark,
Department of Women's and Children's Health,
International Maternal and Child Health,
University Hospital, Uppsala,
Sweden

Date 16/2 2009

TABLE OF CONTENTS

LIST OF TABLES -----	vii
LIST OF FIGURES -----	xi
ACKNOWLEDGEMENTS -----	xii
ABSTRACT -----	xiii
1 Introduction -----	1
1.1 Demography of the menopause-----	2
1.2 Ovarian and hormonal changes of the menopause-----	2
1.3 Definition and staging of the menopause-----	6
1.4 Menopausal symptoms-----	7
1.4.1 Vasomotor symptoms-----	9
1.5 Actions of estrogen-----	9
1.5.1 Effects of estrogens on the central nervous system-----	11
1.6 Impairment of postural balance following the menopause-----	12
1.7 Relevance to Sri Lanka-----	13
1.8 Objectives of the study-----	14
1.8.1 General objectives-----	14
1.8.2 Specific objectives-----	15
2 Literature review -----	16
2.1 Menopausal symptoms –assessment and prevalence-----	16

2.2	Health related quality of life and the menopause-----	19
2.3	Postural balance, reaction time and the menopause-----	20
2.3.1	<i>Assessment of postural balance</i> -----	20
2.3.2	<i>Postural balance and the menopause</i> -----	21
2.3.3	<i>Reaction time and the menopause</i> -----	23
2.4	Menopause and cognition-----	23
2.4.1	<i>Role of estrogen on cognition</i> -----	23
2.4.2	<i>Cognitive functions and the menopause</i> -----	25
2.5	Auditory Brainstem Responses and the menopause-----	27
3	Methodology -----	29
3.1	Study design and area of study-----	29
3.2	Study population-----	29
3.3	Sampling method for the study-----	31
3.3.1	<i>Selection of women by clusters</i> -----	31
3.4	Administration of questionnaires-----	32
3.5	Menopause Rating Scale (MRS) -----	33
3.6	Short Form 36 (SF-36) health survey-----	34
3.7	Classification of menopausal status-----	35
3.8	Selection of the subsample-----	35
3.9	Assessment of the subsample-----	36
3.9.1	<i>Assessment of postural balance</i> -----	36
3.9.2	<i>Reaction time assessment</i> -----	38

3.9.3	<i>Assessment of cognitive functions</i> -----	39
3.9.4	<i>Mini Mental State Examination (MMSE)</i> -----	40
3.9.5	<i>Rey Auditory Verbal Learning Test (RAVLT)</i> -----	40
3.9.6	<i>Assessment of Auditory Brainstem Responses (ABR)</i> -----	41
3.10	Procedure in assessment of the subsample-----	42
3.10.1	<i>Collection of blood samples for assessment of serum hormone levels</i> -----	43
3.10.2	<i>Assessment of serum estradiol concentration</i> -----	43
3.10.3	<i>Assessment of serum sex hormone-binding globulin (SHBG) levels and calculation of the free estradiol index</i> -----	45
3.11	Ethical considerations-----	45
3.12	Statistical analysis-----	46
4	Results -----	47
4.1	Background characteristics of the study population-----	47
4.2	Prevalence and severity of menopausal symptoms-----	49
4.3	The relationship between socio-demographic factors and presence of menopausal symptoms-----	54
4.4	Relationship between menopausal status and quality of life----	63
4.5	Relationship between menopausal symptoms and quality of life-- -----	71
4.6	Characteristics of the subsample-----	75

4.7	The relationship between menopausal stage and performance in balance tests, reaction time tests and cognitive function tests-----	76
4.7.1	<i>The effect of background characteristics of the study subsample on performance in balance tests, reaction time tests and cognitive function tests in relation to menopausal status-----</i>	<i>80</i>
4.8	The relationship between Auditory Brainstem Responses (ABR) and menopausal stage-----	89
4.8.1	<i>The effect of age of the subsample on Auditory Brainstem Responses (ABR) in relation to menopausal status-----</i>	<i>93</i>
4.9	The relationship between serum estradiol levels and performance in balance tests, reaction time tests and cognitive function tests-----	95
4.10	The relationship between serum estradiol levels and ABR latencies-----	97
4.11	The relationship between free estradiol levels and performance in balance tests, reaction time tests and cognitive function tests-----	98
4.12	The relationship between free estradiol levels and ABR latencies-----	104
5	Discussion-----	106
5.1	Characteristics of the study population-----	106
5.2	Prevalence of menopausal symptoms-----	107
5.3	Relationship of symptoms to menopausal status-----	112

5.4	Relationship of menopausal symptoms to socio-demographic factors-----	114
5.5	Relationship between menopausal status and health related quality of life-----	116
5.6	Relationship between menopausal symptoms and the quality of life-----	119
5.7	Relationship between menopausal status / serum estradiol levels and the functional balance tests and reaction time tests-----	121
5.8	Relationship between menopausal status / serum estradiol levels and the cognitive function tests-----	127
5.9	Relationship between menopausal status / serum estradiol levels and the auditory brainstem responses (ABR)-----	130
5.10	Limitations of the study-----	133
6	Conclusions-----	135
7	Recommendations and future directions-----	137
8	References-----	140
9	List of Appendixes-----	155
9.1	Appendix 1 – Communications based on the study-----	155
9.2	Appendix 2 – List of Gramaseva Niladari (GN) divisions of the Kesbewa Divisional secretariat area selected for the study-----	156
9.3	Appendix 3 – Socio-demographic questionnaire-----	157

9.4	Appendix 4 – Menopause Rating Scale (MRS)-----	159
9.5	Appendix 5 – Short Form 36 (SF-36) questionnaire-----	161
9.6	Appendix 6 – Data sheet for functional balance tests-----	165
9.7	Appendix 7 – Mini Mental State examination (MMSE)-----	166
9.8	Appendix 8 – Rey Auditory Verbal Learning test (RAVLT)-	168
9.9	Appendix 9 - Volunteer consent form for participation in subsample study-----	170

LIST OF TABLES

Table 4.1 - Background characteristics of the study population (n=683).....	48
Table 4.2 – Percentage of women complaining of menopausal symptoms measured by the Menopause Rating Scale (n=683).....	50
Table 4.3 – Percentage of women with menopausal symptoms compared between pre-, peri- and postmenopausal groups.....	51
Table 4.4 – Proportion of women with positive scores in the 3 subscales of the MRS compared among pre-, peri- and postmenopausal groups	52
Table 4.5 – Proportion of women with moderate to severe symptoms compared among pre-, peri- and postmenopausal groups	53
Table 4.6 – Menopausal symptoms compared with age of the women.....	55
Table 4.7 – Percentage of women with positive scores in any of the 3 subscales of the Menopause Rating Scale (MRS) compared among the 3 age categories.....	56
Table 4.8– Menopausal symptoms compared among the 3 educational levels of the women.....	57
Table 4.9 – Menopausal symptoms compared with chronic illness	58
Table 4.10 – Relationship between presence of chronic illness and a positive score for the Menopause Rating Scale (MRS) subscales.....	59

Table 4.11- Relationship between the occupational category and presence of a positive score for the Menopause rating scale (MRS) subscales	60
Table 4.12 - Relationship between the parity of the women and presence of a positive score for the Menopause rating scale (MRS) subscales.....	60
Table 4.13- Results of the logistic regression analysis for presence of a positive score for each of the subscales of the Menopause Rating Scale (MRS).....	62
Table 4.14 - Comparison of the mean scores (SD) for each of the 8 domains of the SF-36 among pre-, peri- and postmenopausal groups	64
Table 4.15 - The relationship between the SF-36 quality of life scores and age of the women	65
Table 4.16 - The relationship between the SF-36 scores and chronic illness	66
Table 4.17 - Results of the logistic regression analysis comparing a high score with a low score (below the 25 th percentile) for each of the SF-36 domains	69
Table 4.18 - Results of the logistic regression analysis comparing a high score with a low score (below the 25 th percentile) for each of the SF-36 domains	70

Table 4.19 - The mean (SDs) SF-36 scores compared between women with and without selected menopausal symptoms	72
Table 4.20 - Mean SF-36 scores compared with a positive score in the Menopause Rating Scale (MRS) subscales.....	74
Table 4.21 -The relationship between the functional balance tests and the menopausal stage.....	76
Table 4.22 -The relationship between the reaction times and the menopausal stage.....	79
Table 4.23 - The relationship between the cognitive function tests and the menopausal stage.....	80
Table 4.24 - Relationship between age and performance in reaction time and functional balance tests	81
Table 4.25 - Relationship between age and performance in the cognitive function tests.....	82
Table 4.26 - Relationship between educational level and performance in cognitive function tests.....	83
Table 4.27 - Relationship between the Body Mass Index (BMI) and the performance in reaction time and functional balance tests.....	85
Table 4.28 Relationship between the presence of hot flushes and performance in the reaction time and functional balance tests	87

Table 4.29 – ABR of the right ear in relation to the menopausal stage.....	89
Table 4.30 – ABR of the left ear in relation to the menopausal stage	90
Table 4.31 – The relationship between the Auditory Brainstem Responses for the right ear and the age of the women	93
Table 4.32 – The relationship between the Auditory Brainstem Responses for the left ear and the age of the women.....	94
Table 4.33 - The relationship between serum estradiol level in postmenopausal women and performance in the functional balance tests ...	96
Table 4.34 - The relationship between serum estradiol level and performance in the reaction time tests.....	96
Table 4.35- The relationship between serum estradiol levels and performance in cognitive function tests	97
Table 4.36- The relationship between serum estradiol levels and ABR latencies of the right ear	97
Table 4.37 - The relationship between serum estradiol levels and ABR latencies of the left ear	98
Table 4.38 - The relationship between free estradiol index (FEI) and performance in the functional balance tests.....	99
Table 4.39 - The relationship between free estradiol index (FEI) and performance in the reaction time and cognitive function tests	100

Table 4.40 – Results of the regression analysis for performance in the functional balance tests	102
Table 4.41 – Results of the regression analysis for performance in cognitive function tests.....	104
Table 4.42- The relationship between free estradiol index and ABR latencies of the right ear	105
Table 4.43 - The relationship between free estradiol index and ABR latencies of the left ear	105

LIST OF FIGURES

Figure 3.1 Map of study area	30
Figure 4.1– Box plots of performance in 3 functional balance tests in relation to menopausal status.....	77
Figure 4.2 – Box plots of the latencies of ABR waves I, IV and V of the left ear in relation to menopausal status	91

ACKNOWLEDGEMENTS

I would like to express my sincere gratitude to all those who contributed to this thesis. I particularly wish to express my thanks to:

Prof. Kumudu Wijewardene, my supervisor for her invaluable guidance and patience in helping me to complete the thesis. I am deeply appreciative of all the support she has given me on this project.

Prof. Tord Naessen, my supervisor for sharing his knowledge of research on the menopause and giving invaluable advice and ideas regarding my research project.

Prof. Gunilla Lindmark, my supervisor for her invaluable advice and guidance.

I deeply appreciate the guidance and support given by my supervisors and would like to express my deep gratitude to them.

I am also deeply grateful to Prof. Karin Edebol Eeg-Olofsson for providing advice on the assessment of auditory evoked potentials in my study and the opportunity to learn about this at the Neurophysiology department of the University of Uppsala, Sweden.

I am deeply appreciative of the support given to me by the Head and staff of the Department of Physiology to carry out my research work.

I would like to express my deep gratitude and thanks to all the women who participated in this research study and to the public health midwives who assisted me in the field study.

I am deeply grateful to the SIDA / SAREC project of the University of Sri Jayewardenepura for providing funding for this research project.

Finally I would like to thank my family for their constant support and encouragement which helped me to complete my research project.

ABSTRACT

Menopausal symptoms, quality of life, postural balance and cognitive functions in a community based population of Sri Lankan women

Himansu Waidyasekera

In Sri Lanka there is less information available regarding the menopausal experience of women compared to that in the West. The present study was conducted to assess the prevalence of menopausal symptoms in a community based population of Sri Lankan women and the relationship between these symptoms and their quality of life. In addition the relationship of menopausal status to changes in postural balance, cognitive function and auditory brainstem responses (ABR) was assessed in a subsample of the selected study population. The relationship between changes in these functions and serum estradiol level was assessed in the postmenopausal women included in the subsample.

The study was of cross sectional design and was conducted on 683 women in the age group of 45 – 60 years living in the Kesbewa Divisional Secretariat (D.S) area in Colombo, Sri Lanka. A cluster sampling method was used for recruitment of the sample. A background questionnaire was used to assess demographic and socio-economic information and menstrual and reproductive history. The Menopause Rating Scale (MRS) was used to assess menopausal symptoms and the Short Form 36 health survey (SF-36) to assess the health related quality of life. All 3 questionnaires were administered through a structured interview to all selected women in the main study. The subsample consisting of 40 premenopausal and 67 postmenopausal women were selected from women recruited for the main study. The following tests were assessed in both the premenopausal

and postmenopausal women included in the subsample: postural balance using functional balance tests; reaction time using the CALCAP reaction time software, general cognitive functions using the Mini Mental State examination test (MMSE), verbal memory cognitive function using the Rey Auditory Verbal learning test (RAVLT) and the auditory brainstem responses (ABR). Serum estradiol levels were assessed in the postmenopausal women included in the subsample.

59.3% of the women in the study were postmenopausal. Over 91% of all women complained of one or more menopausal symptoms. The most prevalent menopausal symptoms were joint and muscular discomfort (74.7%), physical and mental exhaustion (53.9%) and hot flushes (39.1%). Women with menopausal symptoms had significantly lower ($p<0.05$) quality of life scores in most of the SF-36 domains when compared to women without symptoms. In the subsample postmenopausal women showed a significant ($p<0.05$) reduction in postural balance and longer ABR wave latencies compared to the premenopausal women. Higher serum estradiol levels in the postmenopausal women was significantly ($p<0.05$) associated with better performance in the reaction time and verbal memory cognitive function test.

In conclusion women of 45-60 years had a high prevalence of somatic type menopausal symptoms and the presence of these symptoms had a significant ($p<0.05$) association with a decrease in their health related quality of life. Postmenopausal status was associated with impairment in postural balance and delayed neural transmission in the auditory brainstem pathways. The study findings suggest that low serum estradiol levels in postmenopausal women may have a role in impairment of postural balance and cognitive functions.