4.1 PHASE 1

Baseline Survey

The study population comprised women (n=1000) aged between 30-60 years from urban area of Vadodara district. Further it was divided into five different zones for screening; east, west, north, and south and central. An equal number of women were enrolled from each zone for the screening of menopause phase. For enrolment of women, an institutional based approach was carried out through ICDS, so that we could get a mix population including all ethnic groups who represent the lower to middle income group population.

4.1.1 Socio demographic profile of the Subjects (N=1000)

All subjects were categorised as per STRAW (Stages of reproductive Aging Workshop) classification which revealed, 58.7% (587) had normal menstrual cycle pattern, 14.6% (146) was passing through perimenopause phase and 26.7% turned up to their post-menopause phase (Table 4.1).

Table 4.1: Distribution of subjects based on the stages of reproductive lifewith mean age of each group (N=1000)

Menopause stage	Frequency	Percent	Mean age (SD)	Median Age
Premenopause (Normal menses)	587	58.7	40.07 (3.79)	40.00
Perimenopause	146	14.6	41.72 (4.28)	41.00
Postmenopause	267	26.7	46.40 (5.32)	47.00
Total	1000	100.0	42.00 (5.10)	41.00

The mean age of the study population was 42±5.10; where mean age of premenopausal group was 40.07±3.79, perimenopausal group was 41.72±4.28 and post menopausal group was 46.40±5.32.

Ahsan et al (2015) reported in his study carried out in Patna, that the mean age of perimenopausal group was 43.45(2.02) and that of postmenopausal group was 48.52 (2.27); where both values were lower in our study.

Chuni N et al (2011) conducted a study in the Nepalese women and reported the mean age of premenopausal women was 45.1 (2.78), perimenopausal women was 49.14 (2.01) and in postmenopausal women it was 55.67 (5.6).

Table 4.2: Distribution of subjects based on their education and profession

Education	**Frequency (N)**	**Percent (%)**
Illiterate	297	29.7
Upto 7	361	36.1
Upto 12	312	31.2
>12 or Graduate	30	3.0
Profession	**Frequency (N)**	**Percent (%)**
Working	796	79.6
Housewife	204	20.4
Total	1000	100.0

Their education profile revealed, 30-36% had completed primary or secondary level schooling and only 3% had completed their graduation, though majority of the women (80%) were working as a maid, salesgirl, peon, gruhudyuog, etc (Table 4.2).

The Kruskal-Wallis test was performed to determine the difference between the distributions of work (profession) across different menopausal stages. There was no significant difference for work distribution across all menopausal transition (p=0.212). This is suggestive that general work situations did not bring any specific impact on reproductive status in these women population.

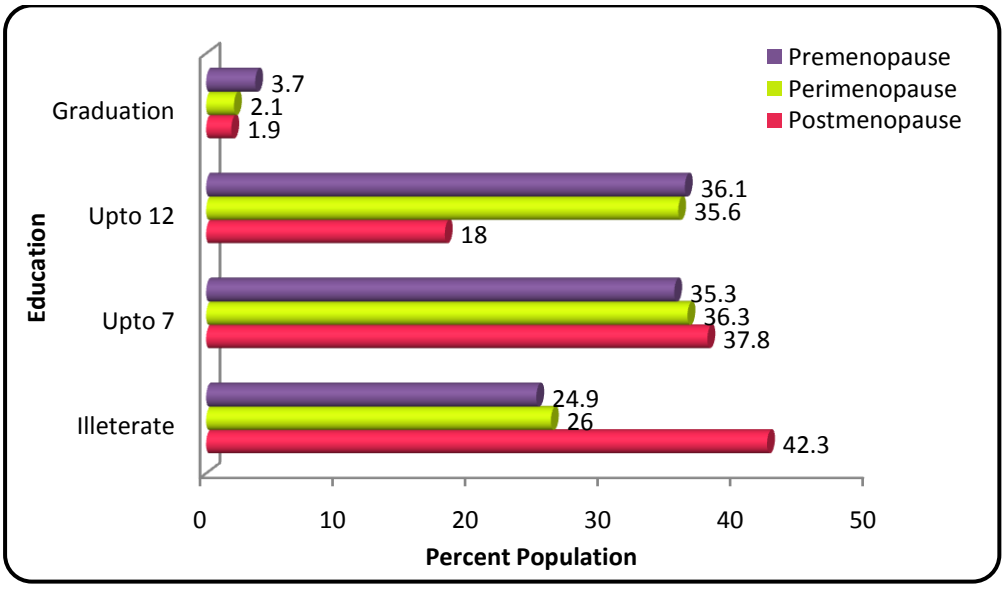


Figure 4.1: Distribution of subjects based on their Education and menopausal stage

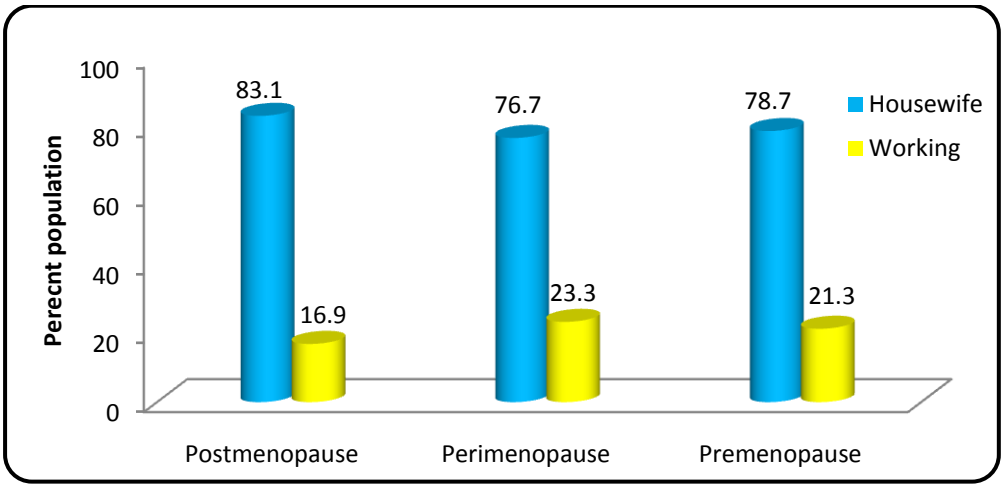


Figure 4.2: Menopausal stage of subjects with respect to their profession

The other observation in the study population, the younger population was more educated than the elders ($p<0.001$); this indicates that the current generation is more aware and concerned with respect to their education which may bring impact on healthy lifestyle.

Looking to their family history, 47% had ≤ 2 children and 45% had 3-4 children and half of the women, 53.6% had experienced pregnancy ≥ 3 times (Table 4.3). The parity numbers were high amongst elderly ($p<0.001$) (Figure 4.3, 4.4).

Table 4.3: Distribution of subjects based on parity numbers (n=1000)

NUMBER OF CHILDREN	FREQUENCY (N)	PERCENT (%)
0 (No child)	33	3.3
1-2	473	47.3
3-4	445	44.5
>4	49	4.9
Total	1000	100.0
NUMBER OF PREGNANCY	**FREQUENCY (N)**	**PERCENT (%)**
0 (No pregnancy)	24	2.4
1-2	294	29.4
3-4	536	53.6
>4	146	14.6
Total	1000	100.0

The more number of pregnancies at times may adversely affect to overall health of a woman. It can be also observed from the data that the younger population believe in small family and more aware and concerned which could be attributed to their nature of work involved in daily lifestyle.

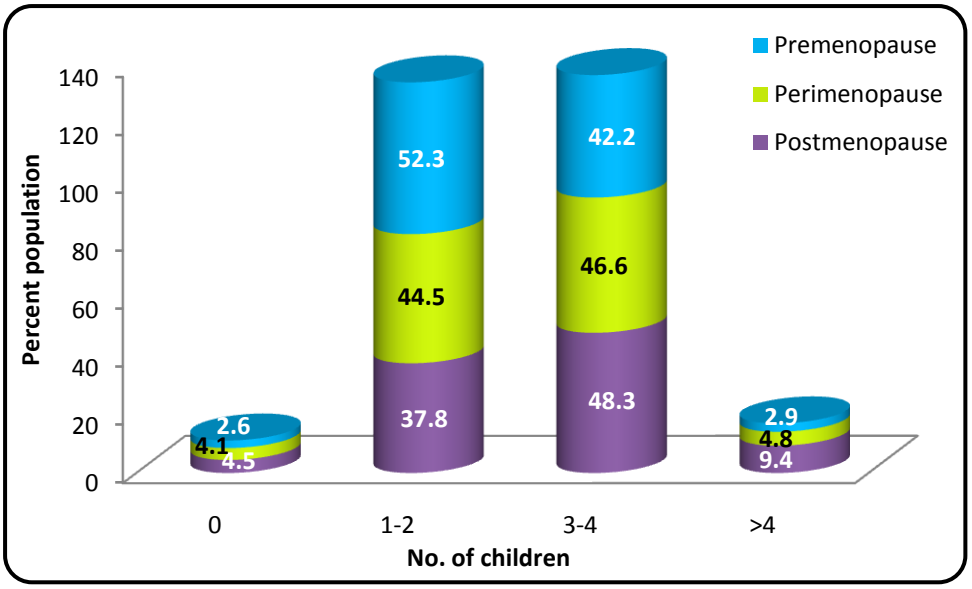


Figure 4.3: Distribution of subjects based on the number of children along with their menopausal stage

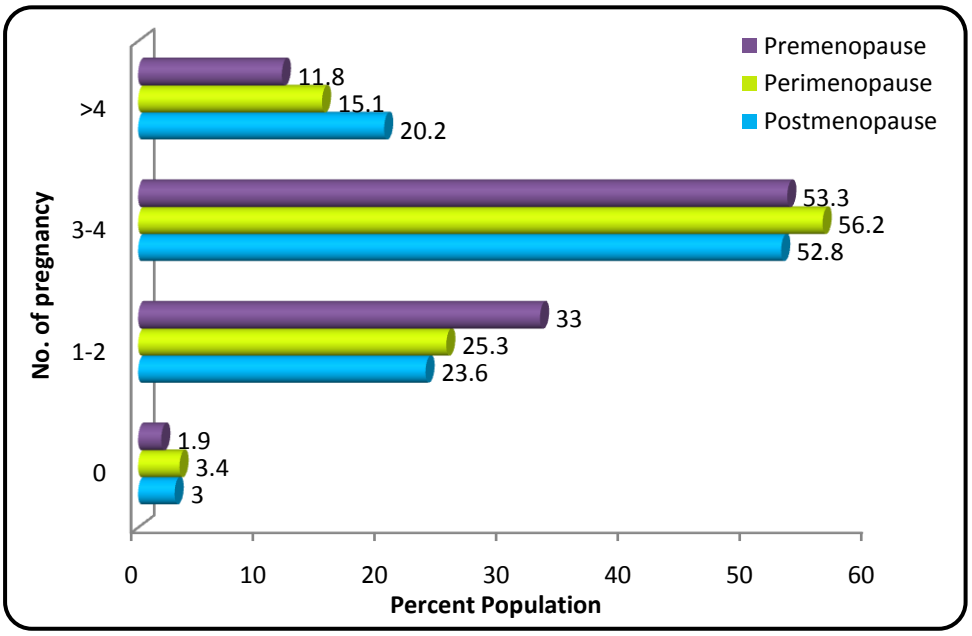


Figure 4.4: Distribution of population based on the number of pregnancy undergone by the women

The self reporting medical history were also collected from the women, which revealed 2.5% suffered from thyroid disorder, 25.3% suffered from blood pressure and amongst all, only 14.4% were on medication (Table 4.4). On further probing it was understood that the subject were reluctant to undergo medication for blood pressure due to the feeling they have to be then on continuous medication.

Table 4.4: Self reporting medical history of the population (n=1000)

Particulars	Yes (%)	No (%)
Thyroid Disorder	25 (2.5)	975(97.5)
Blood Pressure	253(25.3)	747(74.7)
Medication	144(14.4)	856(85.6)

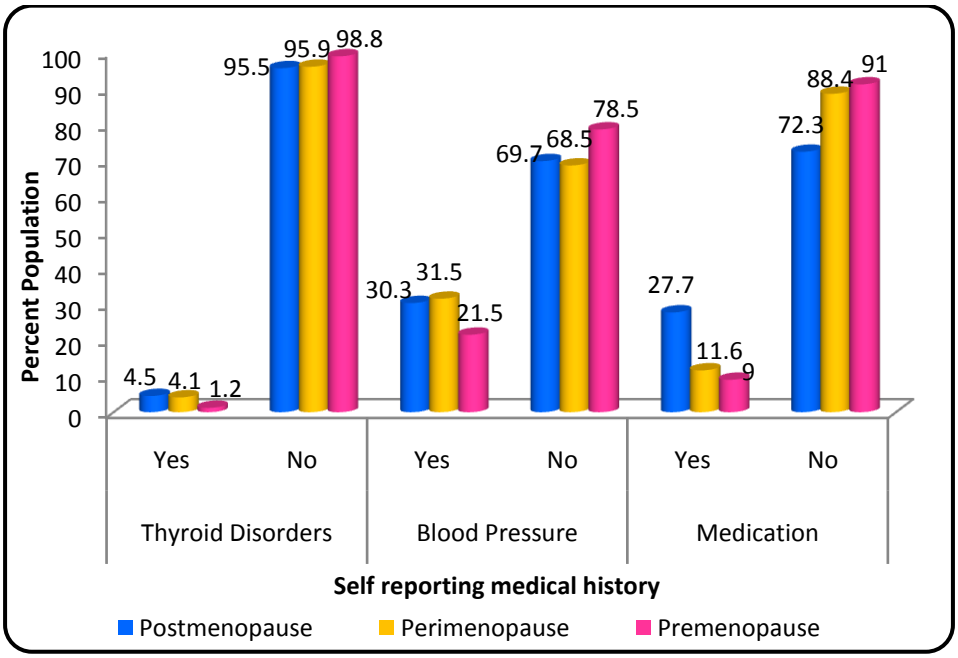


Figure 4.5: Self reporting medical history of population along with their menopausal stage

Self reporting medical history did not show any significant difference with respect to their menopause stage, though thyroid disorders was most prevalent among postmenopausal women (4.5%) followed by

perimenopausal (4.1%). Blood pressure fluctuation was more reported by women in perimenopause (31.5) followed by postmenopausal women (30.3) (Figure 4.5). The premenopausal women reported least medical complications. Variation in percent difference between perimenopause and post menopause was negligible, but it showed that the derangements of hormones of reproductive system, may affect thyroid hormone balances, and women become more prone to thyroid disorders in later stages of life.

4.1.2 Knowledge of the subjects on menopausal health and issues (N=1000)

The information in order to understand their level of knowledge regarding menopause, phytoestrogen, hormone replacement therapy etc. were collected (Table 4.5). The data revealed that 80.8% women were aware and had the knowledge about menopause, but very few knew about what is hormone replacement therapy (0.9%), how the menopause is coupled with thyroid hormones (0.6%) or bone health (1.2%).

Sixty six percent women were familiar with the term iodised salt. The most miserable finding was almost all the women had never heard about phytoestrogen and only 31.5% knew about what is calcium.

There were no significant differences observed in the knowledge of women across the different stages of menopause or as they aged.

Table 4.5: Knowledge of the population (n=1000)

Particulars	Yes (%)	No (%)
Awareness about menopause	808(80.8)	192(19.2)
Awareness about HRT	9 (0.9)	991(99.1)
Awareness about Iodised salt	662(66.2)	338(33.8)

Awareness about Calcium	315(31.5)	685(68.5)
Awareness about Phytoestrogen	2(0.2)	998(99.8)
Relation of thyroid and menopause	6(0.6)	994 (99.4)
Relation of menopause and bone	12(1.2)	988(98.8)

Kaur, Walia and Singh (2004) reported that the 84% of women in north India had prior knowledge about menopause and the most surprising fact in the study was about 47% of the women reported that they were prepared in advance for menopause, 67% of women had discussed menopause with their friends, 78% had discussed it with their husbands. Such knowledge and awareness were lacking in our study population.

Further, in our study we found only 0.9% women had heard of HRT, this finding is comparable to the studies carried out by Shaheen et al (2015) amongst women from Pakistan (10.57% were aware of HRT), Ande et al (2011) in Nigeria, Agwu et al (2008) in rural African communities and Lam et al (2003) among Hong Kong Chinese women.

Dutta et al (2012) in a rural area of Tamilnadu reported only 3.2% women had ever heard of HRT before.

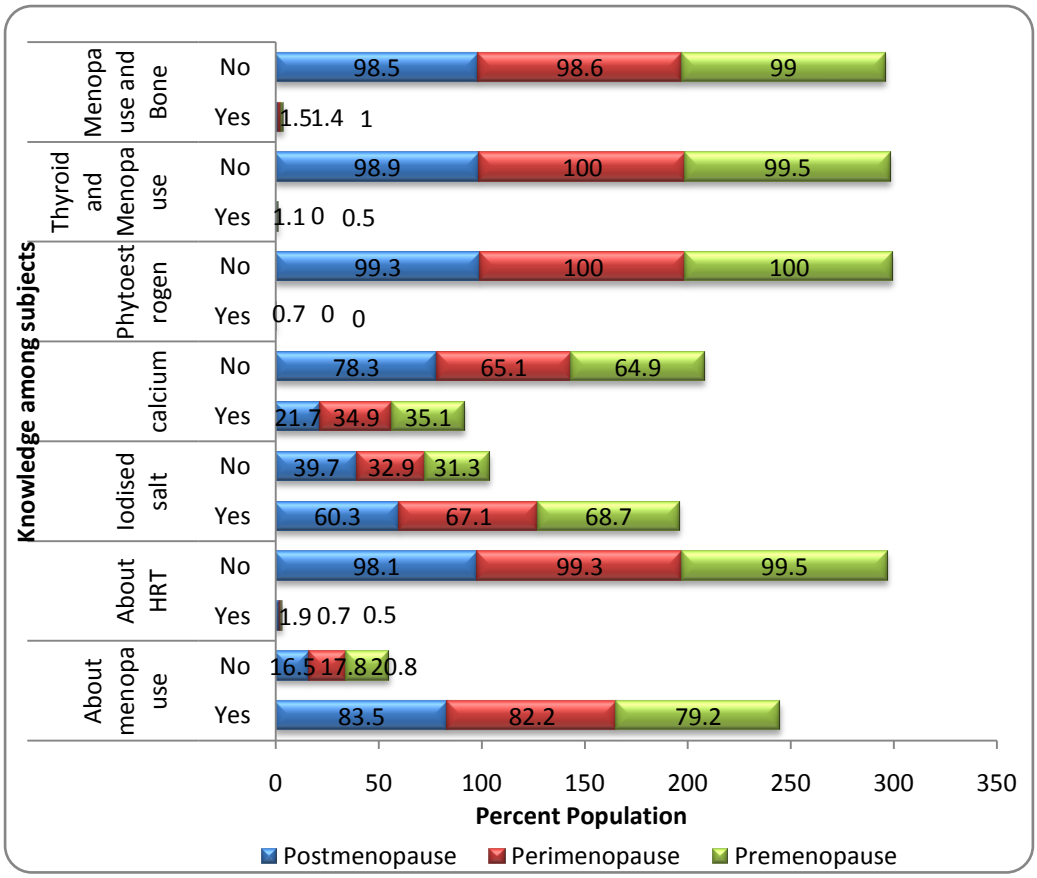


Figure 4.6: Distribution of population based on knowledge and their menopausal stage

The data suggesting that, women are generally unaware of the changes happening in body as aging occurs.

The possible consequences or symptoms occurring during menopause were discussed. Majority of women (89%) did not have any specific idea (Figure 4.7). From rest (n=110, 11%), half of the women said aging is one of the symptoms for menopause transition. Other possible symptoms reported by them were irregular menses (2.6%), impaired vision (3.3%) and abdominal pain during menses (1%). (Figure4.7)

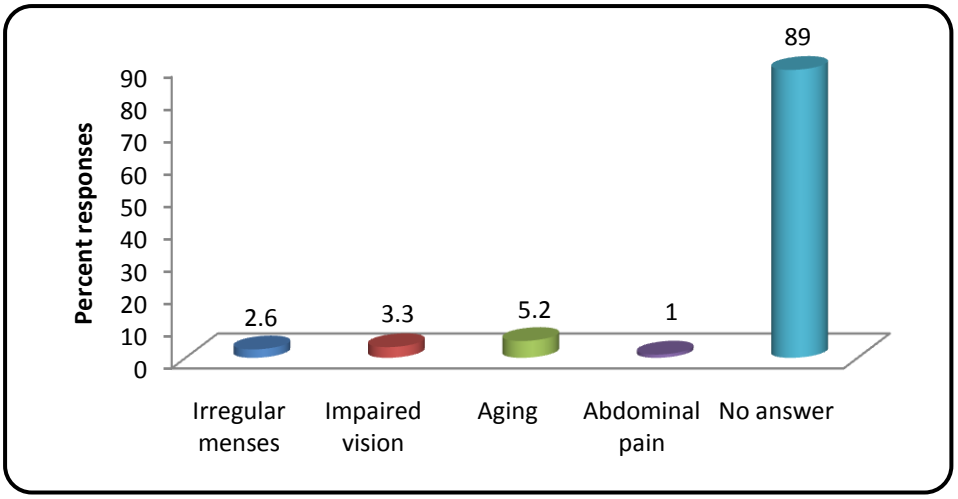


Figure 4.7: Perceptions of the population for menopausal symptoms (n=1000)

Table 4.6: Perceptions of the population for menopausal symptoms at different stages of menopause

Particulars	Irregular menses (%)	Impaired vision (%)	Aging (%)	Abdominal pain (%)	No answer (%)
Premenopause	2.4	3.2	5.2	0.8	88.3
Perimenopause	3.3	5.3	6	0	85.3
Postmenopause	2.6	2.2	4.5	2.6	88.1

In reporting the symptoms, there were no marked differences observed between different menopausal transitions (Table 4.6). The data clearly marks the knowledge regarding menopausal symptoms was poor in the population.

A few more responses were elated from the study population regarding perception on thyroid symptoms. The data revealed that symptoms due to thyroid gland abnormalities which include swelling (13.4%), weight

fluctuation (8.9%) or voice change (1.1%), reported by study population and 78% did not give any response (Figure 4.8).

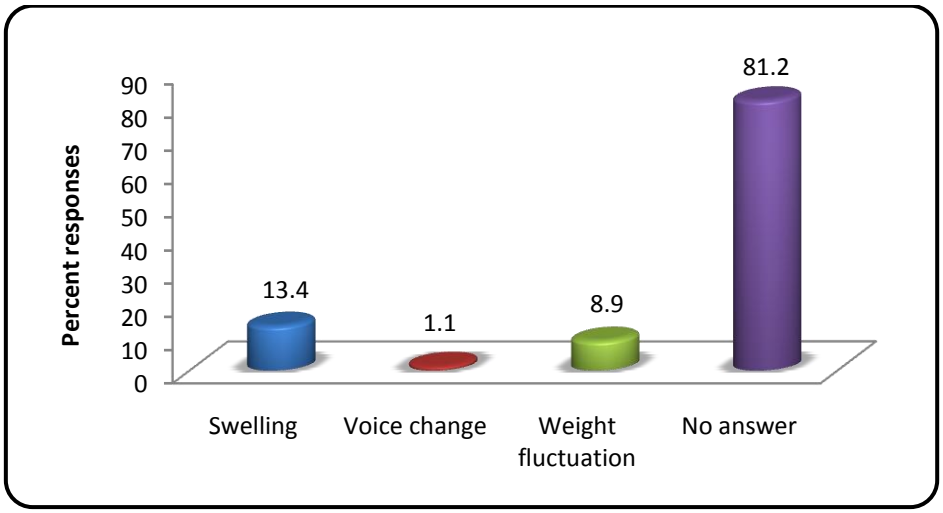


Figure 4.8: Perceptions of the population for thyroid symptoms (n=1000)

Table 4.7: Perceptions of the population for thyroid symptoms at different stages of menopause

Particulars	Swelling (%)	Voice change (%)	Weight fluctuation (%)	No answer (%)
Premenopause	14	0.8	8.2	77
Perimenopause	12.8	0.6	10.3	76.3
Postmenopause	9.7	1.8	8.3	80.1

Further perceptions of the population during various stages of menopause with reference to thyroid were checked. Table 4.7 is suggestive that there was no marked difference observed between different menopausal transitions.

Lack of knowledge and poor perception level of women about menopause and associated health factors may worsen the health quality of middle age women.

4.1.3 Prevalence of menopause related symptoms (N=1000)

The menopausal symptoms experienced by Indian women vary in comparison to the women of western countries. In fact, there are variations within different regions of the country.

WHO has documented that, the majority of women experience months or years of irregular bleeding and variable cycle length before menses cease and that 10% of women stop menstruating abruptly without any such transitional change. (Kaur, Walia and Singh, 2004)

Table 4.8: Percent prevalence of menopausal symptoms in the population

Symptoms	Percent Prevalence			
	Yes			No
Hot flashes	220(22)	Mild	169 (76.8)	780(78)
		Moderate	46 (20.9)	
		Severe	5 (2.3)	
Heart Discomfort	450 (45)	Mild	395 (87.8)	550 (55)
		Moderate	51 (11.3)	
		Severe	4 (0.9)	
Sleep problems	254 (25.4)	Mild	210 (82.7)	746 (74.6)
		Moderate	38 (15)	
		Severe	6 (2.3)	
Mood swings	355 (35.5)	Mild	272 (76.7)	645 (64.5)
		Moderate	77 (21.7)	
		Severe	6 (1.7)	

(Contd.)

Symptoms	Percent Prevalence			
	Yes			No
Irritability	328 (32.8)	Mild	285 (86.9)	672 (67.2)
		Moderate	43 (13.1)	
		Severe	-	
Anxiety	674 (67.4)	Mild	437 (64.8)	326 (32.6)
		Moderate	219 (32.5)	
		Severe	18 (2.7)	
Physical and Mental Exhaustion	668 (66.8)	Mild	495 (74.1)	332 (33.2)
		Moderate	165 (24.7)	
		Severe	8 (1.2)	
Sexual problem	245 (24.5)	Mild	231 (94.3)	755 (75.5)
		Moderate	13 (5.3)	
		Severe	1 (0.4)	
Bladder problems	93 (9.3)	Mild	78 (83.9)	907 (90.7)
		Moderate	13 (14)	
		Severe	2 (2.1)	
Dryness of vagina	485 (48.5)	Mild	426 (87.8)	515 (51.5)
		Moderate	55 (11.3)	
		Severe	4 (0.8)	
Pain in hands and legs	736 (73.6)	Mild	549 (74.6)	264 (26.4)
		Moderate	172 (23.4)	
		Severe	15 (2)	
Irregular menses	412 (41.2)	Mild	58 (14)	588 (58.8)
		Moderate	50 (12.1)	
		Severe	38 (9.2)	
		Very severe	266 (64.7)	
Swelling	173 (17.3)	Mild	146 (84.4)	827 (82.7)
		Moderate	20 (11.6)	
		Severe	7 (4)	
Weight fluctuation	163 (16.3)	Mild	151 (92.6)	837 (83.7)
		Moderate	10 (6.1)	
		Severe	2 (1.3)	
Hair loss	828 (82.8)	Mild	254 (30.7)	172 (17.2)
		Moderate	556 (67.1)	
		Severe	18 (2.2)	

(Contd.)

Symptoms	Percent Prevalence			
	Yes			No
Constipation	139 (13.9)	Mild	87 (62.6)	861 (86.1)
		Moderate	37 (26.6)	
		Severe	15 (10.8)	
Visual Problem	131 (13.1)	Mild	123 (93.9)	869 (86.9)
		Moderate	7 (5.3)	
		Severe	1 (0.8)	
Nails Cracking	21 (2.1)	Mild	14 (66.7)	979 (97.9)
		Moderate	7 (33.3)	
		Severe	-	

During the late menopausal transition, a woman may suffer from different psychological, somatic and urogenital symptoms. There are total 11 symptoms from which Menopause Rating Score (MRS) can be calculated. (Heinemann et al., 2003) Apart from these, exposure of the other symptoms namely, irregular menses, swelling, weight fluctuations, hair loss, constipation, visual problems, and nails cracking were also observed in the women.

Symptoms for MRS:

In our study (Table 4.8), the women reported the pain in hands or legs was the most prevalent (73.6%), followed by anxiety (67.4%), and physical and mental exhaustion (66.8%). The other symptoms like dryness of vagina (48.5%), heart discomfort (45%), mood swings (35.5%) and irritability (32.8%) were reported by nearly half of the population. The other symptoms like sleep disturbances (24.5%), hot flashes (22%), and bladder problems (9.3%) were reported by less number of women.

The symptoms were experienced at mild, moderate or severe levels. In our study the severity of symptoms were observed for anxiety (2.7%), heart discomfort (0.9%), sleep disturbances (2.3%), bladder problems (2.1%).

Other Menopause related symptoms:

Amongst other symptoms related with menopause, hair loss was reported by 82.8% women, irregular menses by 41.2%, swelling by 17.3%, weight fluctuation by 16.3%, constipation by 13.9%, visual problem by 13.1% and only 2.1% women were reported with nails cracking. Among these hair loss and constipation experienced were at moderate frequency, rest all experiences were on mild frequency mode.

The Ecuadorian group of REDLINC recently described the hot flashes (68.9%), sleep disturbances (68.4%), depressive mood (55.2%), irritability (51.6%), muscle and joint pain (77%) were the most prevalent symptoms in middle aged women in American countries (Palacios et al., 2010).

The most common symptoms related to menopause reported by Asian women are symptoms that are not directly estrogen dependent. Muscle and joint aches/pains appear to be the predominant symptoms among peri and postmenopausal women in Asia. (Palacios et al., 2010) Among peri- and postmenopausal women in northern India, the most prevalent symptom was muscle and joint pain (55.8%), followed by tiredness or lack of energy (51.2%) and eye problems (49.6%). (Palacios et al., 2010; Kapur et al., 2009)

Another study in North India reported on attaining menopause women experienced were acuity of vision (n=66, 22%), joint pain/body ache and

swelling on body/feet (n=59, 19.8%), high blood pressure (n=22, 7.4%), headache (n=16, 5.4%), hot flashes/burning sensation in feet (n=19, 6.4%), flatulence (n=15, 5%) and sweating (n=9, 3%).

Waidyasekera et al., (2009) also concluded that the most prevalent menopausal symptoms were joint and muscular discomfort (74.7%), Physical and mental exhaustion (53.9%), and hot flushes (39.1%). Mazhar SB and Rasheed S (2009) reported the hot flushes, sleep problems, and joint/muscular discomfort showed a significant ($p<0.05$ for all) increase in prevalence form the premenopause category to the post menopause category.

4.1.4 Women in Premenopause (N=587)

Nowadays, it is well confirmed that menopausal symptoms experienced by women affect their quality of life. The perimenopausal and postmenopausal women have more menopausal complaints compared to premenopausal women. They were noted to complain significantly more of vasomotor, sexual and psychological symptoms compared to premenopausal women. (Rahman et al., 2010)

Symptoms based on MRS:

The most commonly reported symptoms were Pain in hands and legs (68.3%), Anxiety (61.2%), physical and mental exhaustion (60.1%) followed by dryness of vagina (42.8%), Heart discomfort (41.7%). Irritability (29.5%), mood swings (26.7%), and sexual problems (21%) were reported on a moderate frequency while sleep disturbances (16.2%), hot flashes (14%) and bladder problems (7.7%) were reported least frequently (Figure4.9).

Other Menopause related symptoms:

Amongst other symptoms related with menopause, hair loss was reported by 81.8% women, constipation by 13.6%, weight fluctuation by 13.1%, swelling by 11.4%, visual problem by 10.7%, nails cracking by 1.5% and only one woman was reported irregular menses. Among these hair loss and constipation experienced at moderate frequency, rest all experienced on mild frequency (Figure 4.9).

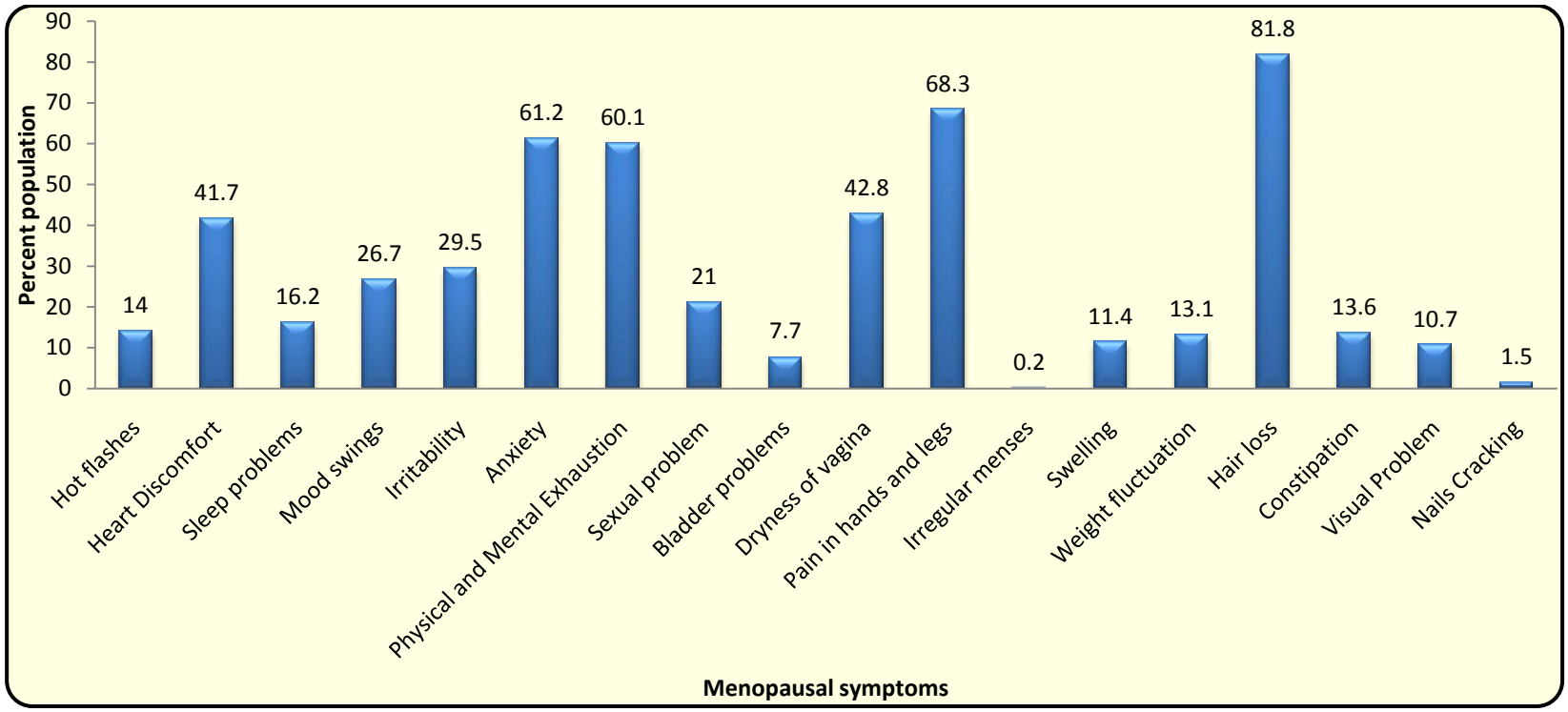


Figure 4.9: Percent prevalence of menopausal symptoms in premenopausal women

Table 4.9: Severity level of menopausal symptoms in premenopausal women

	Percent Population		
Symptoms	**Mild**	**Moderate**	**Severe**
Hot flashes	91.5	8.5	0
Heart Discomfort	89.4	10.2	0.4
Sleep problems	91.6	8.4	0
Mood swings	83.4	15.9	0.6
Irritability	87.3	12.7	0
Anxiety	69.1	29.8	1.1
Physical and Mental Exhaustion	76.5	22.9	0.6
Sexual problem	95.1	4.9	0
Bladder problems	88.9	11.1	0
Dryness of vagina	91.2	8.8	0
Pain in hands and legs	77.3	21.7	1
Irregular menses	0	0	0
Swelling	91	6	3
Weight fluctuation	94.8	3.9	1.3
Hair loss	31.7	65.8	2.5
Constipation	71.2	22.5	6.3
Visual Problem	96.8	3.2	0
Nails Cracking	88.9	11.1	0

The severity level for menopausal symptoms was observed for anxiety, pain in hands and legs, mood swings, physical and mental exhaustion, heart discomfort, constipation, hair loss and weight fluctuation. While majority of the women experienced hot flashes, disturb sleep, irritability, sexual problem, bladder problems, vaginal dryness, at mild and very few were experienced at moderate level (Table 4.9).

4.1.5 Women in Perimenopause (N=146)

Symptoms based on MRS:

The most commonly reported symptoms were Pain in hands and legs (79.5%), physical and mental exhaustion (74.7%), Anxiety (71.9%) followed by dryness of vagina (50.7%), Heart discomfort (50.0%). Mood swings (45.2%), Irritability (39.0%), sleep disturbances (34.9%), sexual problems (30.8%) and hot flashes (28.8%) were reported on a moderate frequency while a bladder problem (7.7%) was reported least frequently (Figure 4.10).

Other Menopause related symptoms:

Amongst other symptoms related with menopause, hair loss was reported by 89% women, weight fluctuation by 27.4%, swelling by 23.3%, visual problem by 18.5%, constipation by 14.4%, and nails cracking by 4.1% of women.

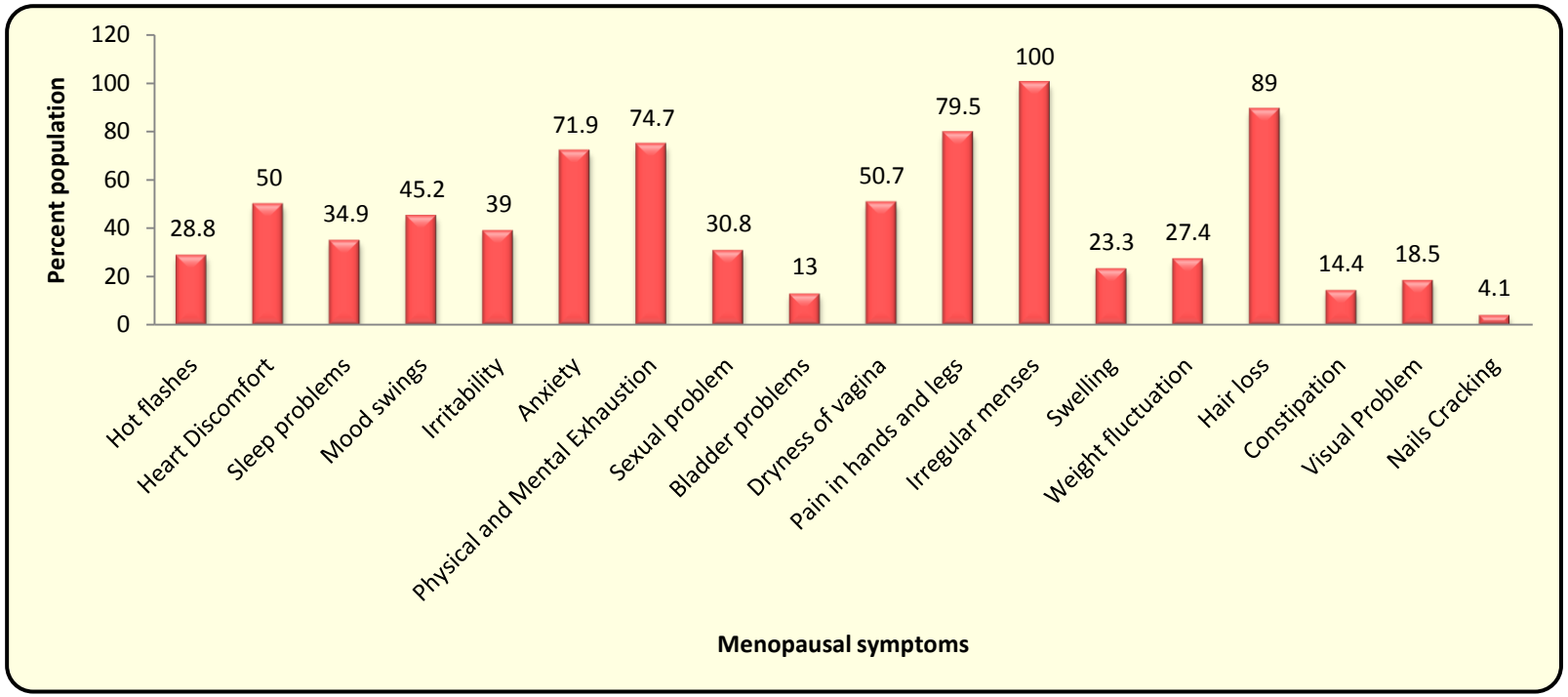


Figure 4.10: Percent prevalence of menopausal symptoms in perimenopausal women

Table 4.10: Severity level of menopausal symptoms in perimenopausal women

Symptoms	Percent Population		
	Mild	Moderate	Severe
Hot flashes	71.4	28.6	0
Heart Discomfort	89	8.2	2.7
Sleep problems	80.4	15.7	3.9
Mood swings	77.3	22.7	0
Irritability	84.2	15.8	0
Anxiety	58.1	38.1	3.8
Physical and Mental Exhaustion	67.9	31.2	0.9
Sexual problem	97.8	0	2.2
Bladder problems	78.9	15.8	5.3
Dryness of vagina	83.8	14.9	1.3
Pain in hands and legs	70.7	28.4	0.9
Irregular menses	39.7	34.2	26
Swelling	79.4	17.6	2.9
Weight fluctuation	92.5	7.5	0
Hair loss	23.9	73.8	2.3
Constipation	61.9	33.3	4.8
Visual Problem	92.6	7.4	0
Nails Cracking	50	50	0

The severity level for menopausal symptoms was seen for bladder problems; disturb sleep, anxiety, heart discomfort, sexual problems, vaginal dryness, pain in hands and legs along with irregular menses, swelling, hair loss and constipation.

While majority of the women experienced hot flashes, mood swings, irritability, swelling, weight fluctuation, constipation and

visual problem at mild and very few were experienced at moderate level (Table 4.10).

Table 4.11: Variables/symptoms to predict perimenopause

Symptoms	OR (CI)	(X^2) p-Value
Swelling	1.56 (1.02-2.38)	**0.038***
Weight Fluctuation	2.24(1.48-3.38)	**0.000*****
Anxiety	1.28 (0.87-1.89)	0.208
Disturb sleep	1.72(1.18-2.5)	**0.004****
Irritability	1.37(0.96-1.98)	0.08
Heart Discomfort	1.26(0.89-1.79)	0.18
Vaginal Dryness	1.1(0.77-1.57)	0.56
Hair loss	1.81(1.05-3.14)	**0.03***
Constipation	1.05(0.63-1.73)	0.85
Visual Problem	1.63(1.02-2.6)	**0.03***
Sexual Problem	1.45(0.99-2.14)	0.05
Hot Flash	1.53(1.03-2.27)	**0.03***
Nail crack	2.39(0.91-6.28)	0.06
Pain in Hands/ legs	1.45(0.95-2.24)	0.08
Mood swings	1.61(1.13-2.3)	**0.008****
Physical and Mental Exhaustion	1.55(1.04-2.31)	**0.029***
Bladder Problem	1.57(0.94-2.4)	0.09

Significantly different at p<0.05, p<0.01**, p<0.001**

On analysis of data – Table 4.11 reveals, the most significant predictors to identify perimenopause stage in women were weight fluctuations, swelling, disturb sleep, physical and mental exhaustion, hot flash, mood swings and, hair loss and difficulties in vision.

4.1.6 Women in Postmenopause (N=267)

Symptoms based on MRS:

The most commonly reported symptoms were Pain in hands and legs (82.0%), physical and mental exhaustion (77.2%), Anxiety (78.7%), dryness of vagina (59.9%) followed by mood swings (49.4%) and Heart discomfort (49.4%), sleep disturbances (40.4%), Irritability (36.7%), hot flashes (36%), and sexual problems (28.8%). While a bladder problems (10.9%) was reported least frequently (Figure 4.11).

Other Menopause related symptoms:

Amongst other symptoms related with menopause, hair loss and weight fluctuation was reported by 81.6% women, swelling by 27%, visual problem by 15.4%, constipation by 14.2%, nails cracking by 2.2% of women while one woman was reported irregular menses.

Mazhar S et al (2009) also reported the less frequent reporting of sexual problems and bladder problems amongst women in Pakistan. He reported the hot flushes (90%) and sleep disturbances (89%) were most common in his study population, which was not similar in our study population.

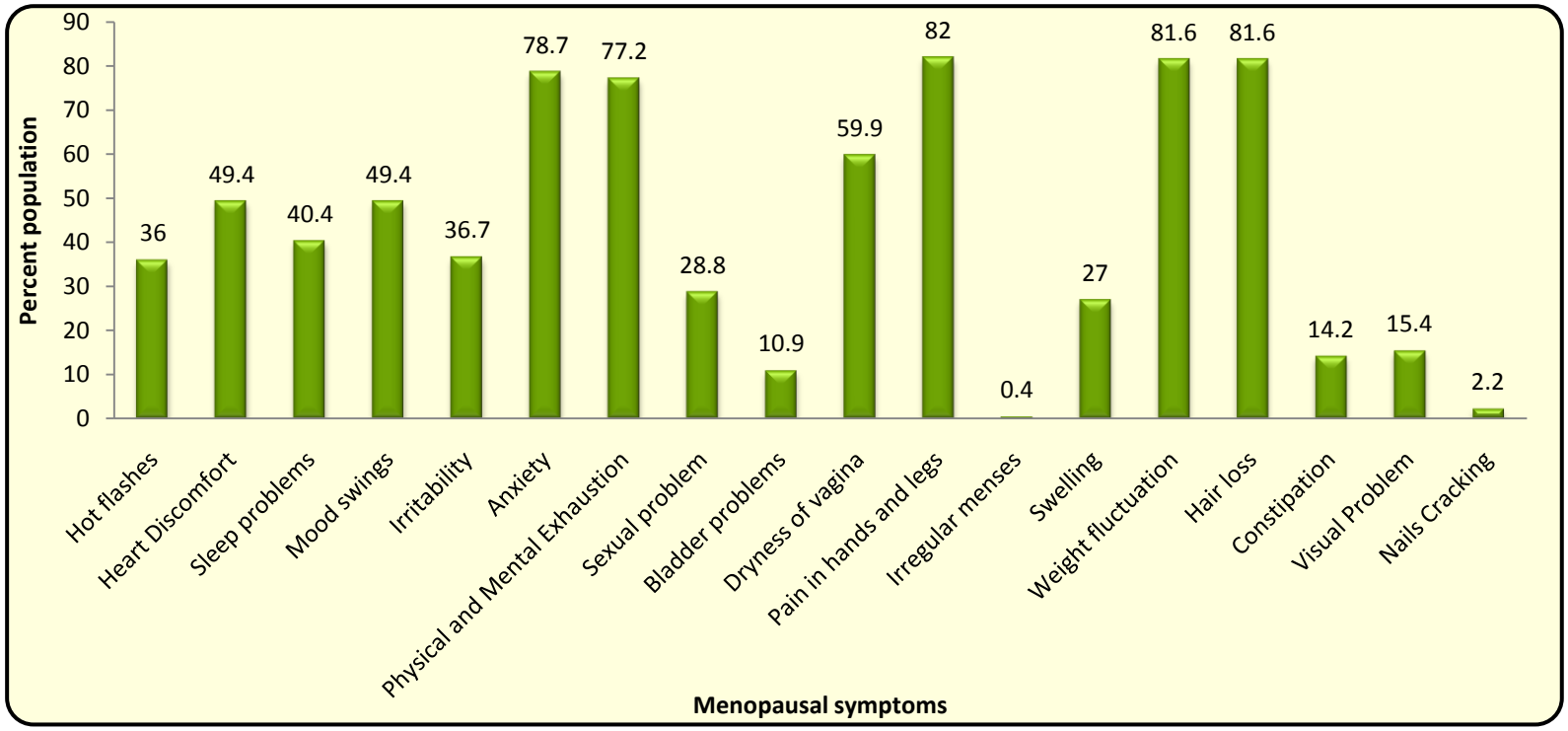


Figure 4.11: Percent prevalence of menopausal symptoms in postmenopausal women

Table 4.12: Severity level of menopausal symptoms in postmenopausal women

	Percent population		
Symptoms	**Mild**	**Moderate**	**Severe**
Hot flashes	66.7	28.1	5.2
Heart Discomfort	84.1	15.2	0.8
Sleep problems	75.9	20.4	3.7
Mood swings	68.2	28	3.8
Irritability	87.8	12.2	0
Anxiety	61	34.3	4.7
Physical and Mental Exhaustion	73.3	24.3	2.4
Sexual problem	90.9	9.1	0
Bladder problems	79.3	17.2	3.5
Dryness of vagina	84.4	13.8	1.8
Pain in hands and legs	71.7	23.7	4.6
Irregular menses	0	0	0
Swelling	80.6	13.9	5.6
Weight fluctuation	89.1	8.7	2.2
Hair loss	32.6	66	1.4
Constipation	44.7	31.6	23.7
Visual Problem	90.2	7.3	2.4
Nails Cracking	50	50	0

Table 4.13: Variables/symptoms to predict postmenopause

Symptoms	OR (CI)	(X^2) p-Value
Swelling	2.31(1.64-3.25)	**0.000*** **
Weight Fluctuation	1.1(0.75-1.59)	0.63
Anxiety	2.13(1.53-2.96)	**0.000*** **
Disturb sleep	2.73(2.01-3.7)	**0.000*** **
Irritability	1.27(0.94-1.7)	0.11
Heart Discomfort	1.27(0.96-1.69)	0.08
Vaginal Dryness	1.88(1.41-2.49)	**0.000*** **
Hair loss	0.89(0.62-1.29)	0.56
Constipation	1.03(0.69-1.55)	0.85
Visual problem	1.29(0.86-1.93)	0.2
Sexual Problem	1.36(0.99-1.86)	0.05
Hot Flash	2.76(2.01-3.78)	**0.000*** **
Nail Crack	1.1(0.42-2.86)	0.84
Pain in Hands/ legs	1.9(1.34-2.7)	**0.000*** **
Mood swings	2.24(1.68-2.98)	**0.000*** **
Physical and Mental Exhaustion	1.98(1.43-2.73)	**0.000*** **
Bladder Problem	1.27(0.8-2.02)	0.3

Significantly different at p<0.05, p<0.01**, p<0.001**

The most significant predictors to identify post menopause stage in women were anxiety, swelling, disturb sleep, physical and mental exhaustion, vaginal dryness, hot flash, mood swings and, pain in hands and legs as observed in Table 4.13.

The present study reported 40% to 60% of premenopausal women also reported similar symptoms (joint and muscular discomfort, physical and mental exhaustion, heart discomfort), this could be

explained since most of the somatic or psychological symptoms experienced by these middle age women are not exclusively as a result of changes due to menopause alone, it's could also resulted from other physical, psychological or health related problems which is related to aging, stressful life, socio-cultural milieu, economic factors, poor dietary and lifestyle practices in these group of women which can represent as menopausal like symptoms. Chuni and Reddy (2011), Rahman et al., (2010) and Harvey et al., (2002) have also reported the similar findings and opined the same.

During transition from perimenopause to postmenopause, we observed the severity of symptoms was increased for hot flashes, mood swings, anxiety, physical and mental exhaustion, pain in hands and legs, swelling, weight fluctuations, constipation and visual problems.

In response to lower estrogen production, the changes in brain neurotransmitters results into hot flashes. It is believed that with time fluctuation in estrogen level decreases so as to severity of hot flashes. (Ahsan et al., 2015) Imbalances in estrogen also affect and increases serotonin level which leads to anxiety and mood swings. In our study population we found increase in severity of these symptoms from perimenopause to post menopause stage, which suggestive that the estrogen fluctuation was not yet stabilised in the study population. As in the current study, the women were in their early phase of post menopause could suffer from this fluctuation, it might be get reduced at later stage of menopause.

Increase in severity of pain in joints/pain in hands and legs in study population could be attributed to worsening of menopause related bone health. This is also indicative of poor diet, low calcium intake and lack of exercise in the current study population.

Other symptoms like weight fluctuation, constipation, and visual problem are not directly estrogen dependent and might be an effect of aging and poor lifestyle practises of population.

The mean of total MRS was found to be stepping up during transition from premenopause (4.60 ± 3.07) to perimenopause (6.53 ± 3.93) and showed again a step down during transition from perimenopause (6.53 ± 3.93) to postmenopause (5.78 ± 3.03). A similar pattern was observed for mean of all three dimensions i.e., Psychological (2.20 ±1.73 to 3.05 ± 1.90 and 3.05 ± 1.90 to 2.81 ± 1.71), Somato-vegetative (1.64 ± 1.24 to 2.40 ± 1.7 and 2.40 ± 1.7 to 2.07 ± 1.31) and Urogenital (0.77 ± 0.88 to 1.08 ± 1.09 and 1.08 ± 1.09 to 0.89 ± 0.90).

Between the three subscales of MRS the mean of the Psychological domain (2.59 ± 1.91) was higher followed by somatic symptoms (2.03 ± 1.54) and the least by the Urogenital symptoms (0.92 ± 0.99). A similar trend was observed for all three subscales during all stages of reproductive life, i.e. premenopausal, perimenopausal or postmenopausal.

Table 4.14: Comparison of Subscales (three different dimensions) and total MRS Score according to the menopausal status (Mean ± SD)

VARIABLE	PREMENOPAUSE (N=587)	PERIMENOPAUSE (N=146)	POSTMENOPAUSE (N=267)	TOTAL POPULATION (N=1000)
Psychological Symptoms	2.20 ± 1.73	3.05 ± 1.90	2.81 ± 1.71	2.59 ± 1.91
Somatic Symptoms	1.64 ± 1.24	2.40 ± 1.7	2.07 ± 1.31	2.03 ± 1.54
Urogenital Symptoms	0.77 ± 0.88	1.08 ± 1.09	0.89 ± 0.90	0.92 ± 0.99
Total MRS	4.60 ± 3.07	6.53 ± 3.93	5.78 ± 3.03	5.54 ± 3.66

Very similar results were reported by Del Prado M, where the higher score was given by the psychological domain (7.7 ± 4.4) followed by the somatic domain (5.8 ± 3.5) and the least by the urogenital domain (2.7 ± 2.9).

Reports from individual countries confirm the wide variation in the prevalence of vasomotor symptoms among Asian women. Women of Chinese origin experienced a lower risk of menopausal symptoms when compared to those of both Malay and Indian ethnic groups ($p < 0.05$). (Palacios et al., 2010)

A relatively higher prevalence of vasomotor symptoms was reported among Indian and Srilankan women. Among 50 perimenopausal Indian women living in Delhi, 32% reported hot flashes, and 24% reported night sweats (Palacios et al., 2010; Gupta et al., 2006).

To understand and confirm the difference in total MRS during pre, peri and post menopause stages, Independent sample Kruskal-Wallis test was performed. This showed a significant difference in MRS for all menopausal transitions ($p<0.001$). Figure 4.12 represents the median value of MRS across pre, peri- and post menopausal women and its statistical significant difference.

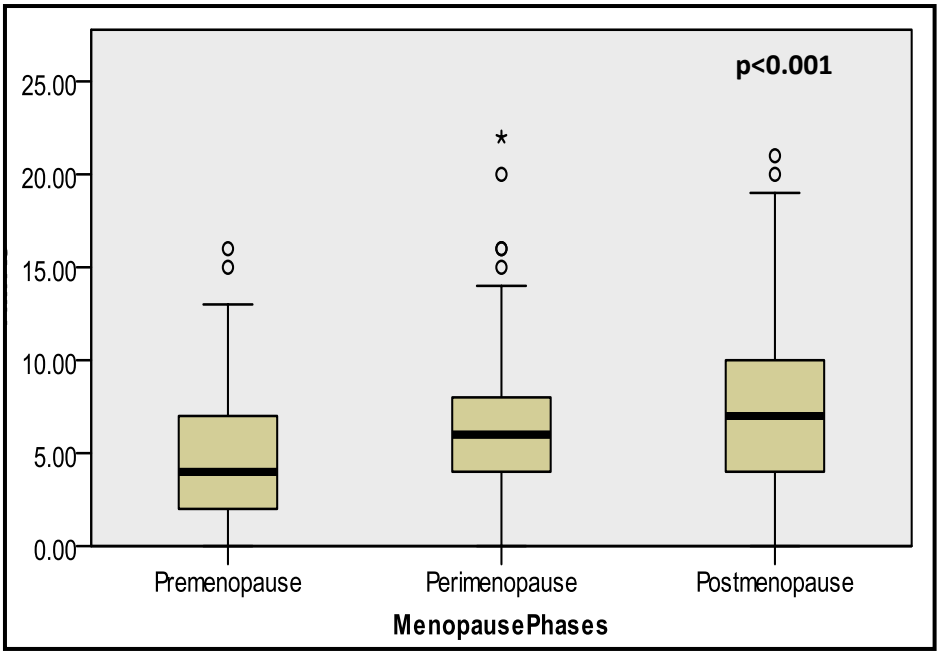


Figure 4.12: Distribution of MRS across menopausal phases

We also observed, scores for all three dimensions were higher in perimenopausal women in comparison to post menopause.

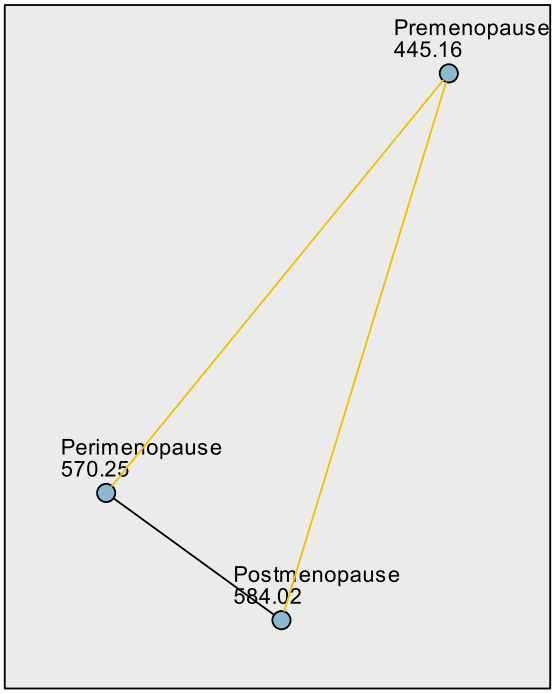
Ahsan et al (2015), reported the mean score for somatic subscale and psychological scale was higher in perimenopausal women in comparison with postmenopausal women. He found statistically significant ($p<0.01$) increase in psychological subscale.

Similar findings were also reported by Rahman et al (2010) in the study among middle age women in Kuching, Sarawak, Malaysia. They reported the somatic and psychological subscales were experienced most by perimenopausal women compared to the post menopausal or premenopausal women and in the urogenital subscale, the postmenopausal women were reported to suffer the most compared to the other two groups. A similar trend was also reported by others (Lu et al., 2007; Peeyananjarassri et al., 2006; Chedraui et al., 2008; Harvey et al., 2002; Dhillon et al., 2005).

Our study reported the urogenital subscale was also greater for perimenopausal women in comparison to postmenopausal women; this finding is contradictory to other studies mentioned above.

Further to understand, the difference between three subscales of MRS across three menopausal transition post hoc analyses was carried out. The results (Figure 4.13, 4.14 and 4.15) revealed that there was a significant difference between premenopausal and perimenopausal for reporting psychological ($p<0.001$), somato-vegetative ($p<0.001$) and urogenital ($p<0.01$) symptoms. Also a significant difference was observed between premenopausal and postmenopausal women for psychological, somato-vegetative and urogenital symptoms ($p<0.001$).

There was no significant difference in reporting these symptoms between perimenopausal and postmenopausal women.

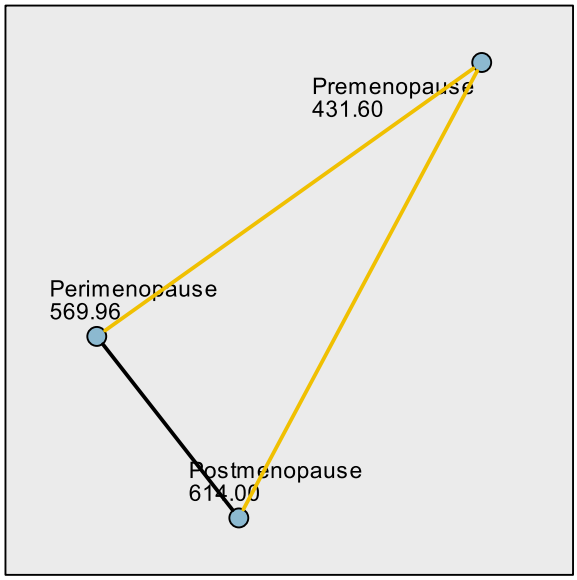


Each node shows the sample average rank of MenopausePhases.

Sample1-Sample2	Test Statistic	Std. Error	Std. Test Statistic	Sig.	Adj.Sig.
Premenopause-Perimenopause	-125.091	26.342	-4.749	.000	.000
Premenopause-Postmenopause	-138.854	21.025	-6.604	.000	.000
Perimenopause-Postmenopause	-13.763	29.318	-.469	.639	1.000

Each row tests the null hypothesis that the Sample 1 and Sample 2 distributions are the same.
Asymptotic significances (2-sided tests) are displayed. The significance level is .05.

Figure 4.13: Pair wise comparison: Score of Psychological Symptoms across menopausal stages

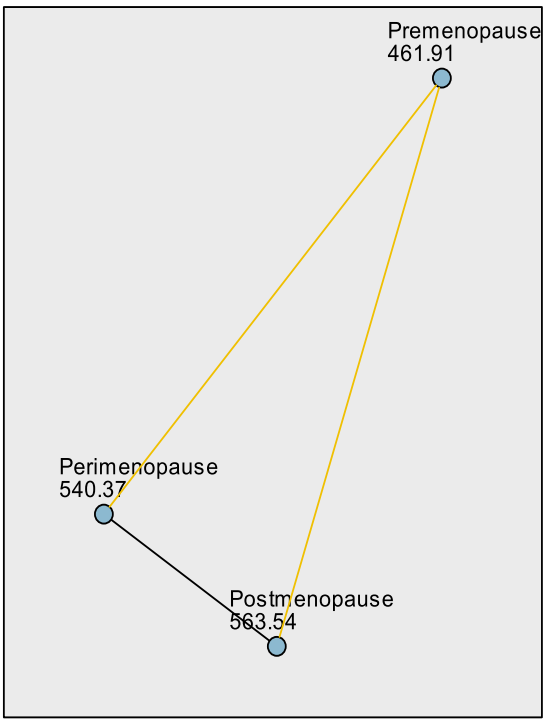


Each node shows the sample average rank of MenopausePhases.

Sample1-Sample2	Test Statistic	Std. Error	Std. Test Statistic	Sig.	Adj.Sig.
Premenopause-Perimenopause	-138.366	26.110	-5.299	.000	.000
Premenopause-Postmenopause	-182.406	20.841	-8.752	.000	.000
Perimenopause-Postmenopause	-44.040	29.060	-1.515	.130	.389

Each row tests the null hypothesis that the Sample 1 and Sample 2 distributions are the same.
Asymptotic significances (2-sided tests) are displayed. The significance level is .05.

Figure 4.14: Pair wise comparison: Score of Somato-vegetative Symptoms across menopausal stages



Each node shows the sample average rank of MenopausePhases.

Sample1-Sample2	Test Statistic	Std. Error	Std. Test Statistic	Sig.	Adj.Sig.
Premenopause-Perimenopause	-78.462	25.076	-3.129	.002	.005
Premenopause-Postmenopause	-101.635	20.015	-5.078	.000	.000
Perimenopause-Postmenopause	-23.173	27.910	-.830	.406	1.000

Each row tests the null hypothesis that the Sample 1 and Sample 2 distributions are the same.
Asymptotic significances (2-sided tests) are displayed. The significance level is .05.

Figure 4.15: Pair wise comparison: Score of Urogenital Symptoms across menopausal stages

Irrespective of the menopausal transition, psychological problems and symptoms were reported higher among women, where society and family members play a major role. This is suggestive that psychological and emotional aspects need to be taken care by the society for betterment of women's health. This study confirms the women face psychological, physiological (somato-vegetative) and urogenital problems since early stages of their mid life and continues in later life, may persist till end of life. These lead to affect and disrupt or worsen the health related quality of mid-life's women.

The world population of women aged over 60 years was below 250 millions in 1960 and it is estimated that in 2030, 1.2 billion women will be peri or postmenopausal and this will increase by 4.7 million a year (Jin YL, 1997).

Modern medicine has significantly increased the life expectancy of women throughout the world. (Cheng MH, 2005).

With the above facts, the current findings point towards the need of an attention towards improvement in health of women in post-reproductive years. Healthcare providers need to create awareness and tailor the available therapy or treatment for betterment of health. The systemic hormone replacement therapy prove beneficial to get relief in vasomotor or psychological symptoms in perimenopausal women but long term use of HRT can lead to breast cancer, changes in the intrauterine lining etc. The situation thus calls for an increasing demand of herbal approach as an alternative. Amongst plant based products a group of compounds - 'Phytoestrogens' mimic actions of estrogen. Active components like isoflavones and flavonoids present in them have synergistic effect of estrogenic and anti-estrogenic activity, e.g. Flaxseeds, etc.

Foods like wild yams, sesame seeds, fenugreek, soybeans etc. are known to mimic estrogenic actions in the body. Hence a multiple food based approach is required to enhance estrogen pool which will not only protect the women from menopause related health issues but at the same time is considered safe to consume.

Therefore it was of interest to observe the phytoestrogenic activities of a few foods in our study. The second phase was designed based on this approach.

4.2PHASE 2

HPLC Analysis of Phytoestrogens - Overview

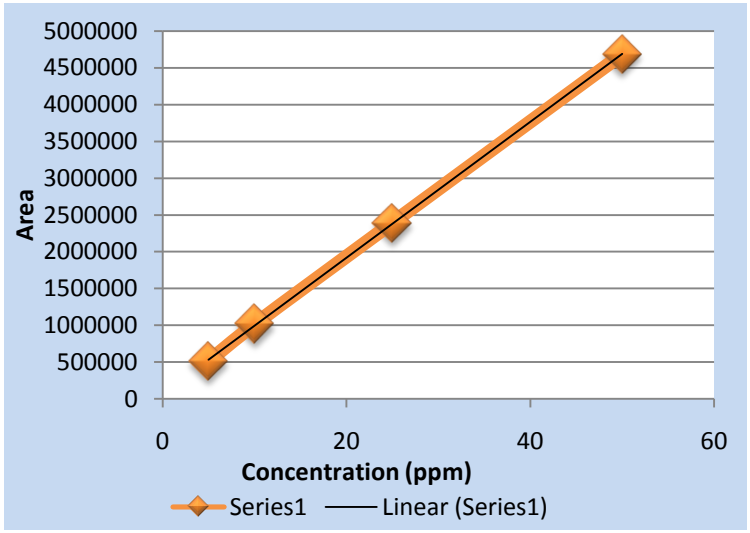
This was an analytical phase of the study, where HPLC analysis was used for the identification and quantification of phytoestrogens present in *Trigonellafoenum-graecum* seeds (common name – Fenugeek, local name - Methi), *Amorphophalluspaeoniifolius* (common name – Elephant yam, local name – Suran), *Punicagranatur*(Common name – Pomegranate, local name – Dadam), and Flaxseeds.

This phase comprised two objectives - Standardization of the method and Identification and quantification of phytoestrogen from all four samples. The standards used for the analysis were Isoflavone (Daidzein and Gensitein), Liganans (Secoisolariciresinol and Matairesinol) and Comestans (Coumestrol).

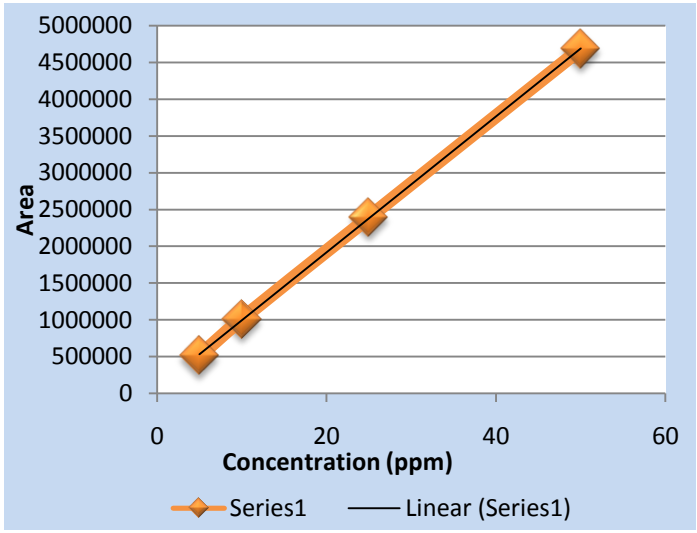
4.2.1 Standardization of method – Analysis of standards

The methods proposed byEliasson C (2003), Griffith AP (2001), and Xin Li (2008) were modified and standardized for the present study.

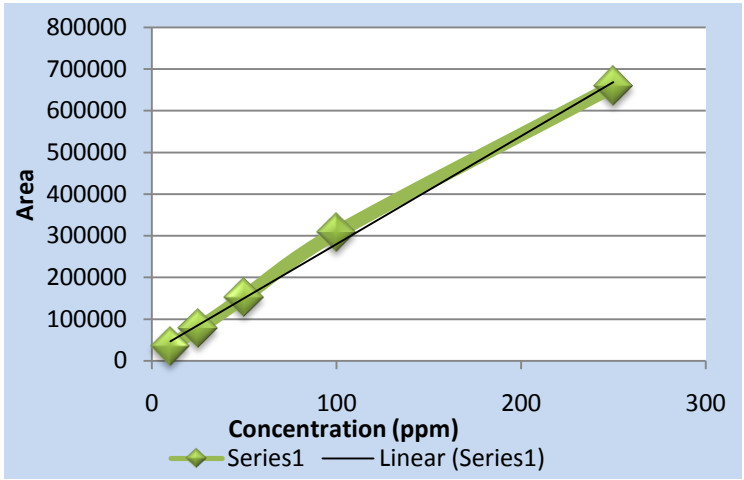
Standard phytoestrogen solutions were prepared by addition of 60% ethanol to purified phytoestrogen to prepare a stock solution (1000 ppm) for all analytes and stored at $\leq 4^{o}$C. For calibration curves, stock solutions were then diluted with ethanol to five different concentrations: For Isoflavone (Daidzein and Gensitein) – 2.5ppm-50ppm; For Liganans (Secoisolariciresinol and Matairesinol) and Comestans (Coumestrol) - 10ppm-250ppm) and duplicate analysis were performed for each concentration.



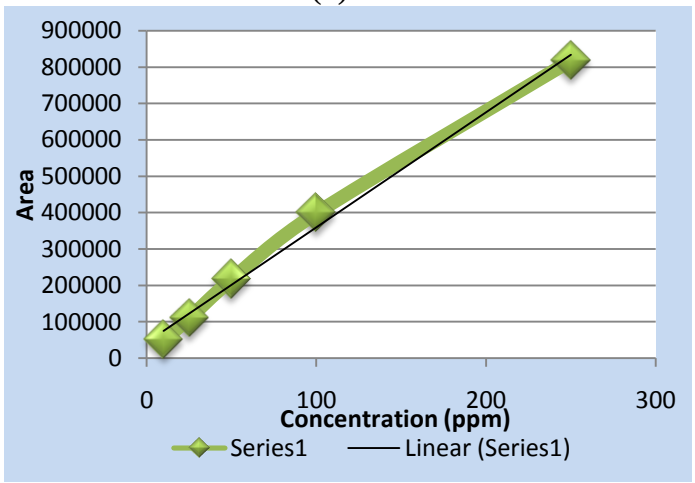
(a) daidzein



(b) Genistein

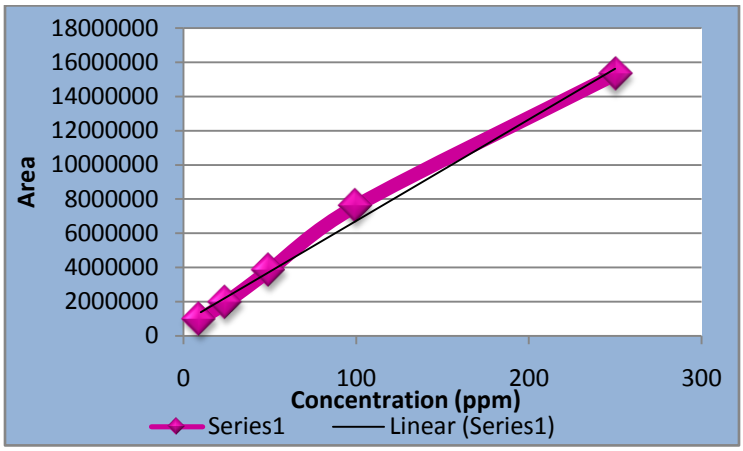


(c) secoisolariciresinol



(d) matairesinol

Figure 4.16: Calibration curves for phytoestrogen standard solutions



(e) Coumestrol

Figure 4.16: Calibration curves for phytoestrogen standard solutions (Contd.)

There different mobile phase compositions employed were Methanol/water, Acetonitrile/water, Acetonitrile/methanol/ammonium acetate buffer, Water/acetonitrile/acetic acid to achieve baseline resolution between all analytes.

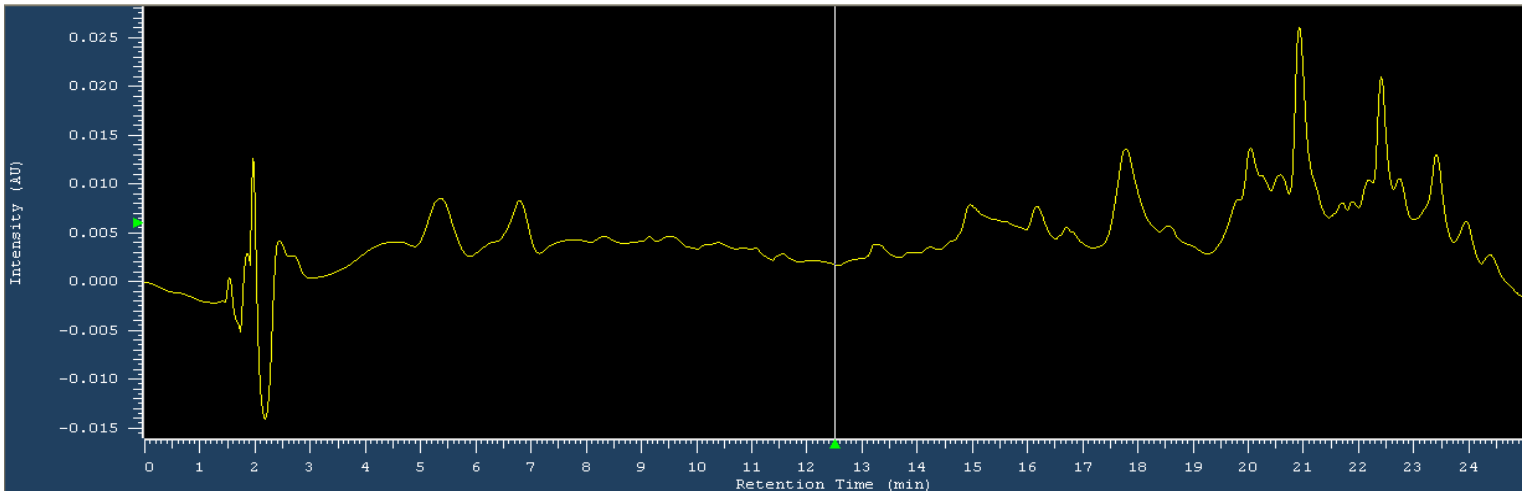
Amongst all, we have found better identification and good resolution with 0.1% (v/v) acetic acid in water and 0.1% (v/v) acetic acid in acetonitrile.

The calibration curves for standard solutions were depicted in Figure 4.16.

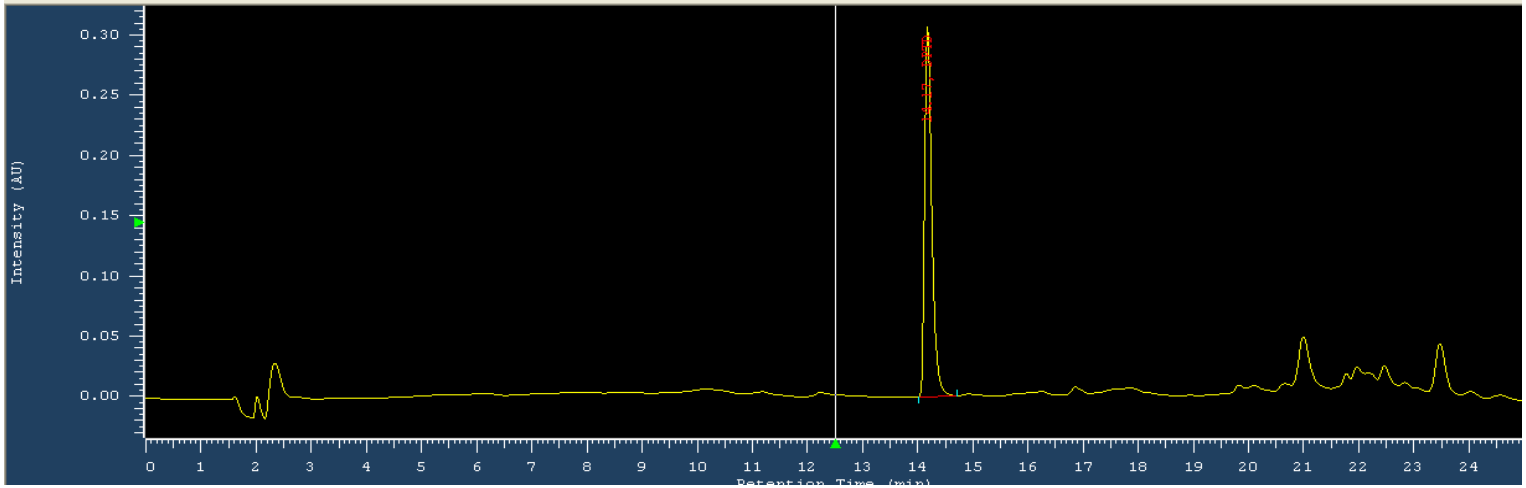
Table 4.15: Analysis of Standard solutions

Sr. No.	Name of Standard	RT	Linear regression equation	r^2
1	Daidzein	14.17	Y=12262X +26565	0.999
2	Genistein	16.06	Y=92355X +72509	0.999
3	Coumestrol	16.71	Y=59379X +77605	0.991
4	Secoisolariciresinol	12.53	Y=2590X + 21033	0.995
5	Matairesinol	15.98	Y=3159X + 43979	0.992

The calibration curves of the peak area against the concentration for selected standards at 245 nm gave good linear responses over a wide range of concentration (Table 4.15, Fig. 4.16)

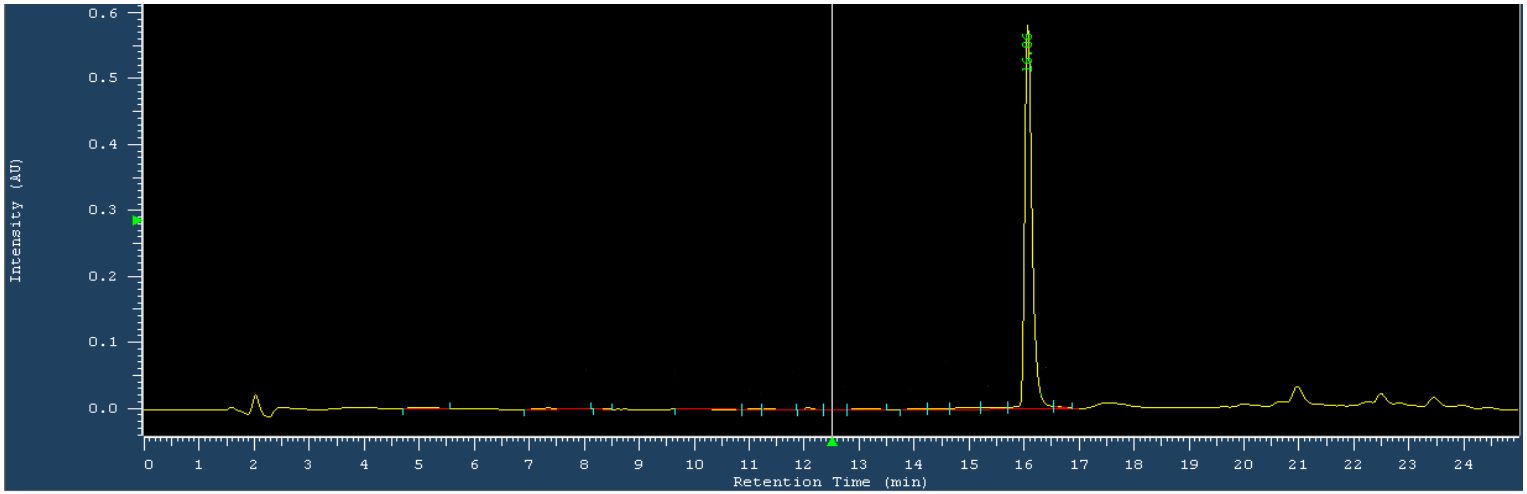


(a) Blank

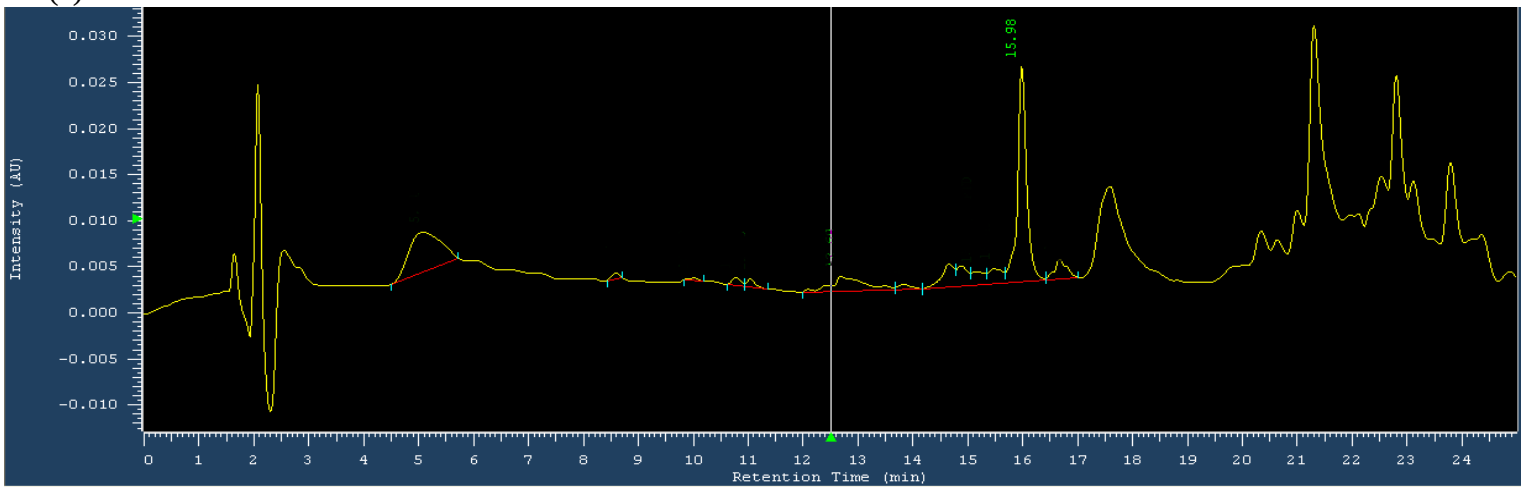


(b) Diadzein

Figure 4.17: HPLC chromatogram for standard solutions

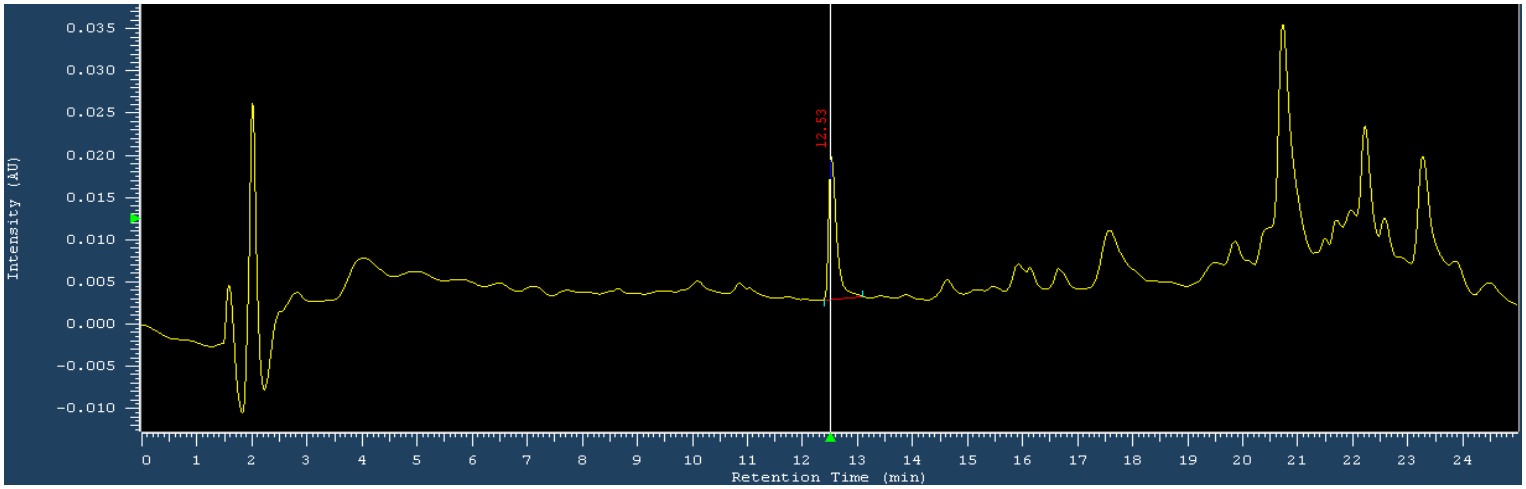


(c) Genistein

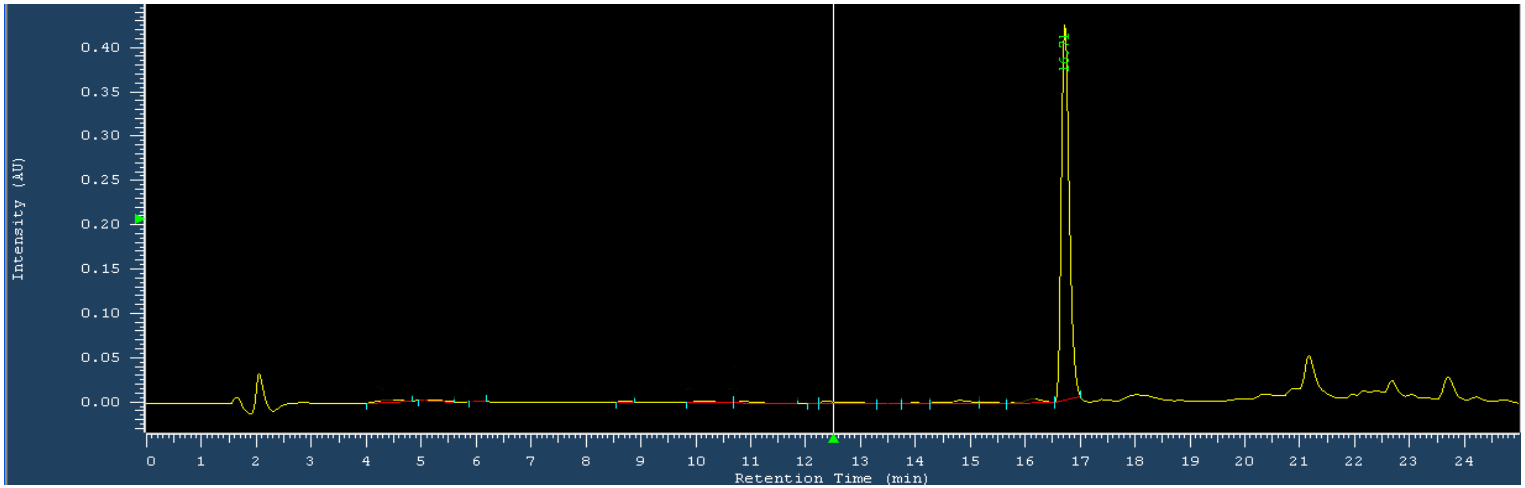


(d) Matairesinol

Figure 4.17: HPLC chromatogram for standard solutions (Contd.)



(e) Secoisolariciresinol



(f) Coumestrol

Figure 4.17: HPLC chromatogram for standard solutions (Contd.)

Figure 4.17 revealed the typical HPLC chromatograms obtained for standard solutions showing peaks corresponding to daidzein (b, RT = 14.17) genistein (c, RT= 16.06), matairesinol (d, RT=15.98), secoisolariciresinol (e, RT=12.53)and coumestrol (f, RT=16.71) and other minor unknown peaks.

4.2.2 Analysis of samples

Various types of sample preparation procedures have been documented for the analysis of phytoestrogens range from "filter and inject" for urine to solvent extraction for foods and tissues, hydrolysis of conjugates for foods and physiological samples. (Wang et al., 2002) In the present study, we used the hydrolysis of conjugates for the analysis of phytoestrogens.

All four food samples were converted into to dry powder form and subjected to extraction. For the extraction of samples, 60% ethanol was used.

As the exact nature and composition of isoflavone glycosides present in foods other than soy is not very much known, all the reported sample preparation protocols utilize a hydrolysis step to form isoflavonoidaglycones. The advanced techniques like GC-MS for phytoestrogen analysis involves a time consuming and complex sample preparation consisting of several solid-phase extraction and chromatographic separation. The simplest sample preparation protocol described until now was for the HPLC-DAD though this involves acidic hydrolysis, reported by Wilkinsin et al., (2002).

Frank et al., (1998) employed similar solvents as we used in the present study, i.e. composition of acetonitrile and acetic acid-water. Thereafter in further studies, they changed this solvent system to methanol and

dichloromethane with acetonitrile as mobile phase. And findings were, though there was a better separation and improvement in limits of detection for equol and O-des-methylangolensin (DMA) with methanol and dichloromethane, these were reduced for analytes like daidzein, genistein and coumestrol. In our study we were focusing on daidzein, genistein and coumestrol, we used composition of acetonitrile and acetic acid-water.

HPLC-DAD is an appropriate technique and newly reported method to show that, the length of the chromatographic run can be reduced to less than 20 min with retention of adequate resolution, as reported by Griffith et al., (2001). (Wilkinsin et al., 2002)

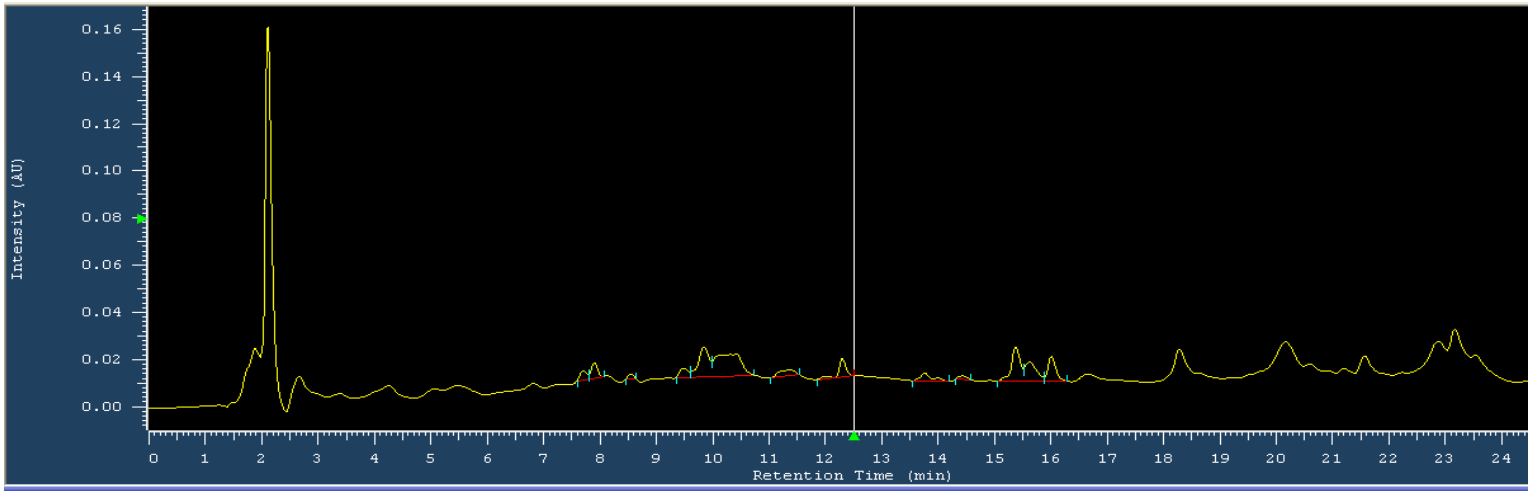
In the present study also, with a proposed method we achieved a good resolution for all analytes with run time less than 20 minutes. Therefore this finding contributes to a major scientific progress where in 20 minutes, we can analyzevarious phytochemical substances.

The studies also reported that under acid hydrolysis conditions, genistein becomes unstable. (Garrette et al., 1999; Franke et al., 1994) And we were also interested in coumestrol; we employed alkaline hydrolysis for the analysis.

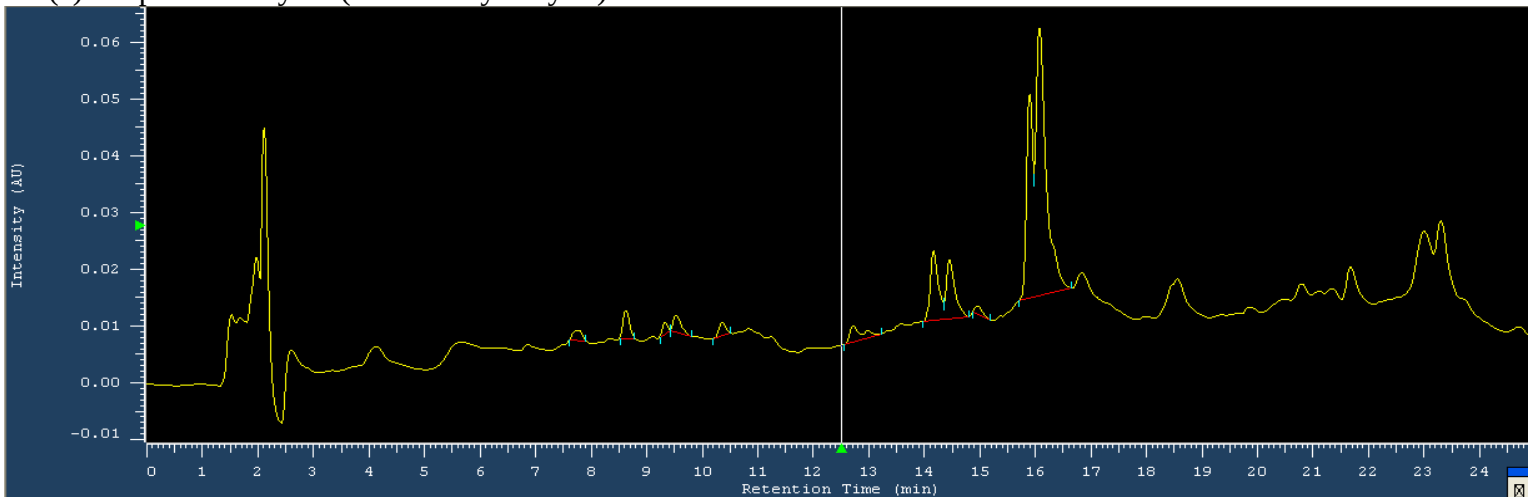
Table 4.16 summarized the identified phytoestrogenic components with their quantification from fenugreek, flaxseeds, pomegranate and yam with and without alkaline hydrolysis following proposed analytical method.

Table 4.16: Phytoestrogen estimation from samples using HPLC

Sr. No.	Name of Sample	RT	Area	Possible compound	Conc^{n} (ppm)
1	Fenugreek	12.39	18865	Secoisolariciresinol	283.66
		13.94	50685	Daidzein	18.17
		16.18	23029	Genistein	11.79
2	Fenugreek Alkaline Hydrolyzed	12.65	125827	Secoisolariciresinol	1893
		13.99	272359	Daidzein	100.96
		15.95	109554	Genistein	56.07
		16.83	281924	Coumestrol	170.12
3	Flaxseed	13.55	1629737	-	-
4	Flaxseed Alkaline Hydrolyzed	12.43	69964	Secoisolariciresinol	1067.4
		14.16	8695	Daidzein	3.27
		16.15	56570	Genistein	29.36
5	Pomegranate	14.28	21491	Daidzein	7.82
6	Pomegranate Alkaline Hydrolyzed	13.99	84197	Daidzein	31.23
		15.99	59493	Matairesinol	562.34
		16.10	59493	Genistein	30.46
7	Yam	16.01	47468	Genistein	24.30
8	Yam Alkaline Hydrolyzed	14.16	57841	Daidzein	21.62
		15.89	127668	Matairesinol	1216.28
		16.07	292108	Genistein	150.76

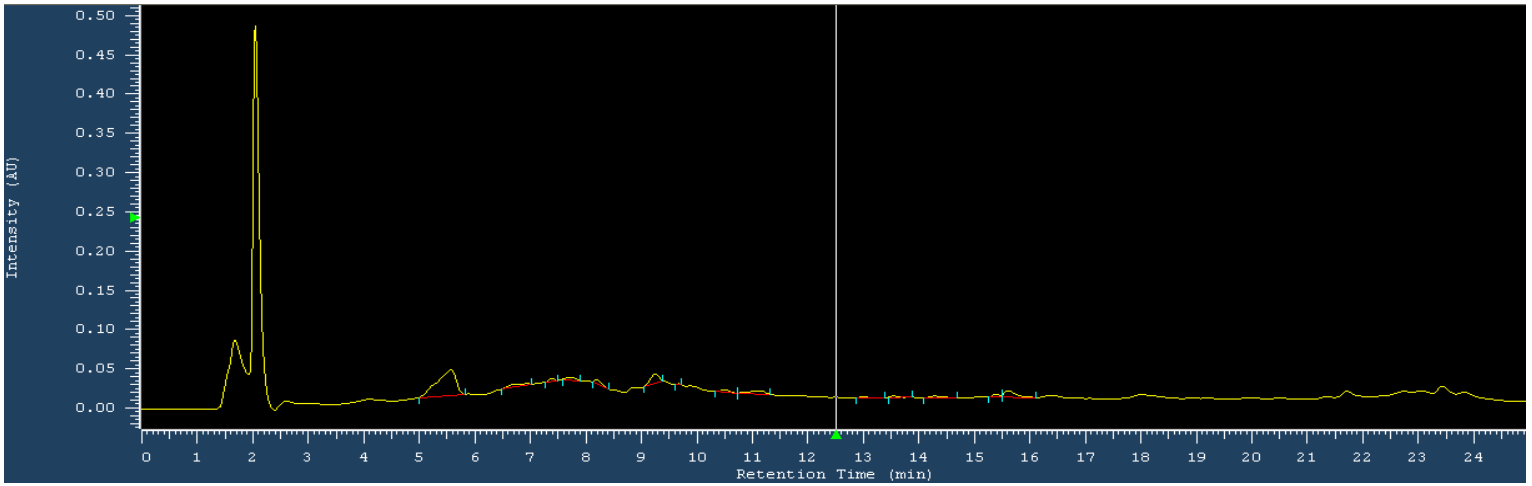


(a) Elephant foot yam (Without hydrolysis)

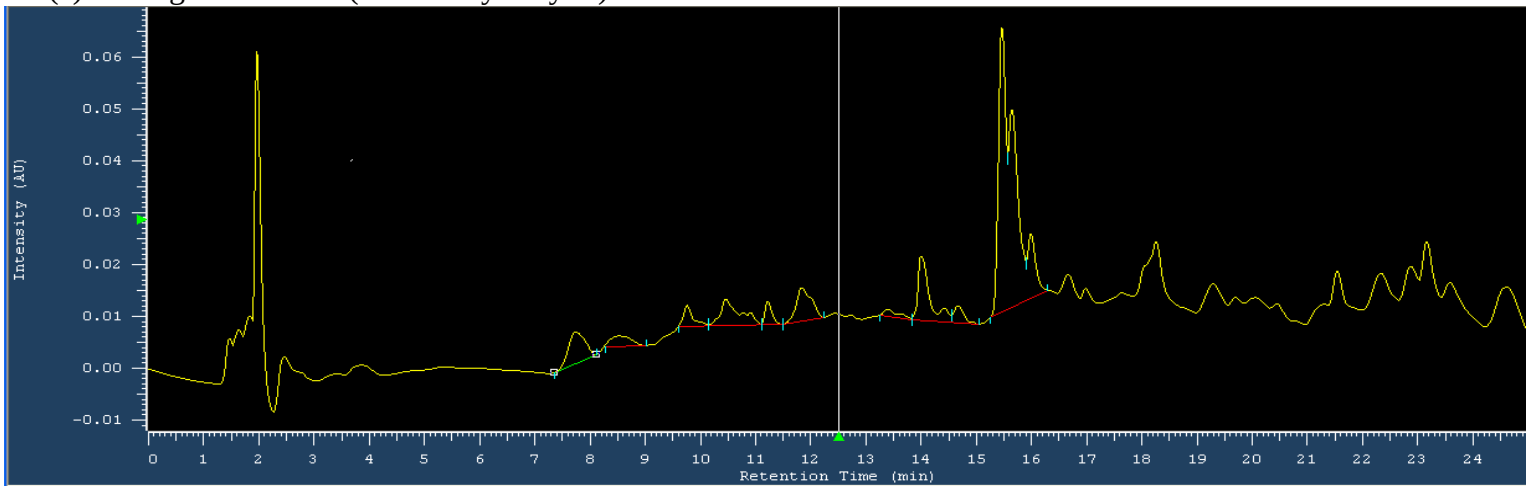


(b) Elephant foot yam (Alkaline Hydrolysis)

Figure 4.18: HPLC chromatogram for phytoestrogen estimation from Elephant foot yam: a) without hydrolysis and b) after alkaline hydrolysis

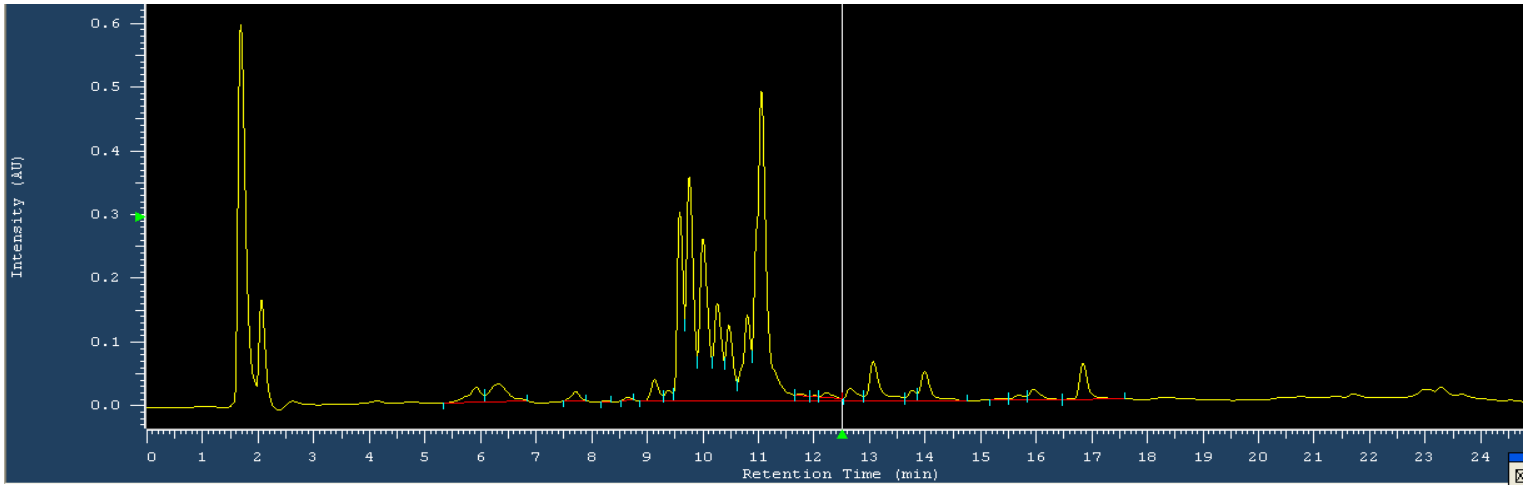


(a) Pomegranate seeds (without hydrolysis)

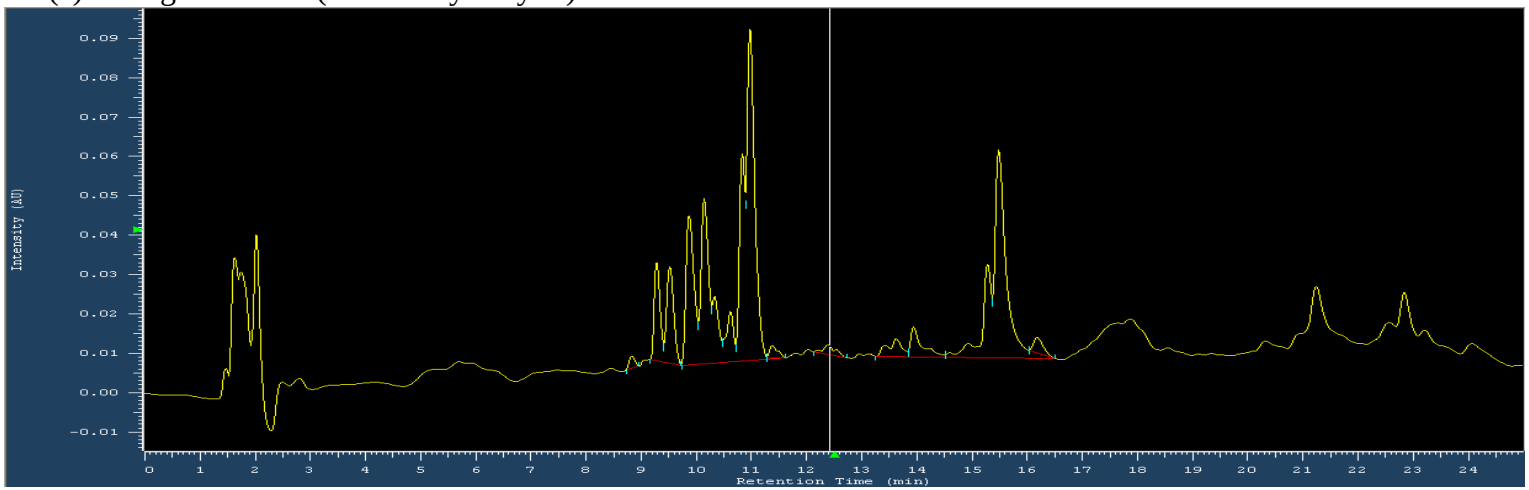


(b) Pomegranate seeds (Alkaline Hydrolysis)

Figure 4.19: HPLC chromatogram for phytoestrogen estimation from Pomegranate seeds: a) without hydrolysis and b) after alkaline hydrolysis

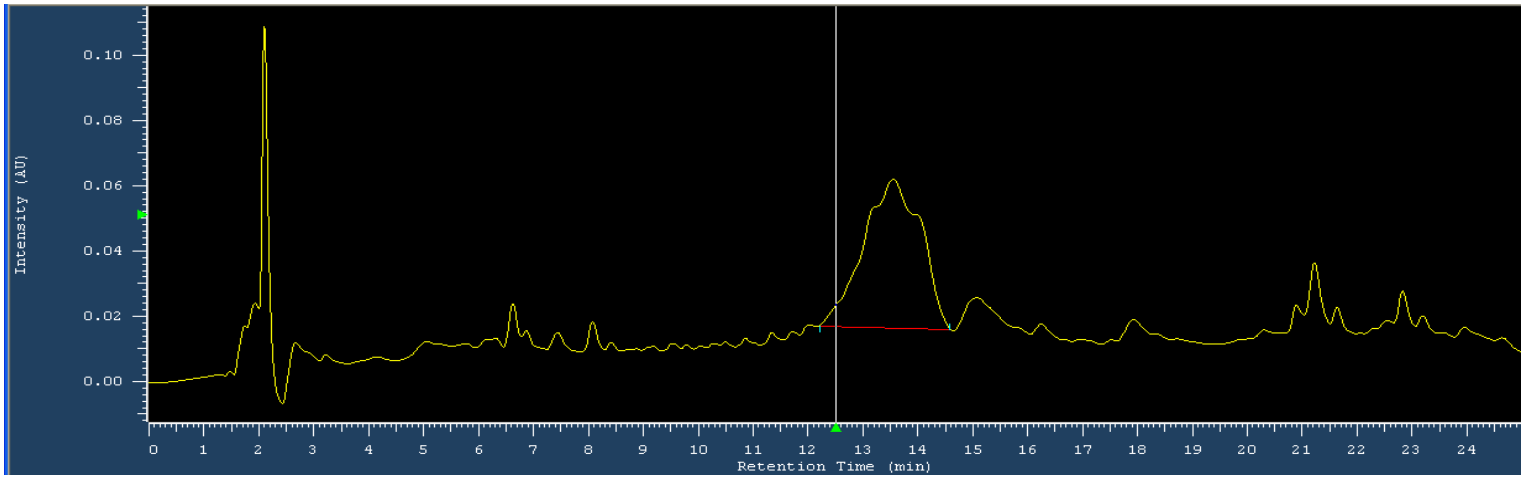


(a) Fenugreek seeds (without hydrolysis)

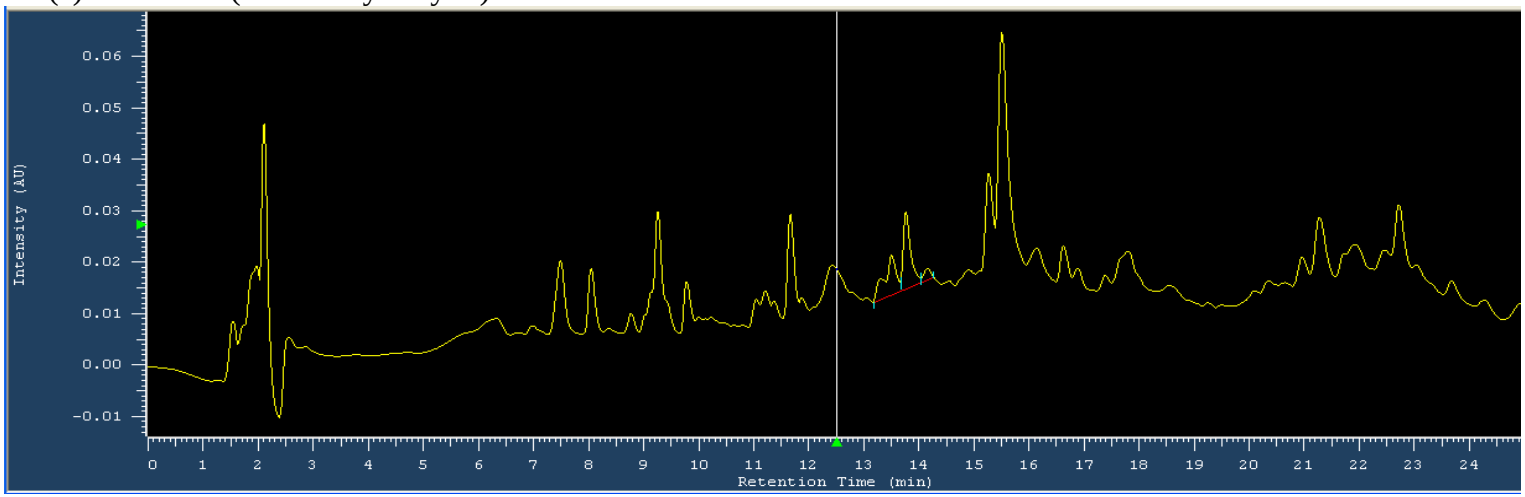


(b) Fenugreek (Alkaline Hydrolysis)

Figure 4.20: HPLC chromatogram for phytoestrogen estimation from Fenugreek seeds: a) without hydrolysis and b) after alkaline hydrolysis



(a) Flaxseeds (without hydrolysis)



(b) Flaxseeds (Alkaline Hydrolysis)

Figure 4.21: HPLC chromatogram for phytoestrogen estimation from Flaxseeds: a) without hydrolysis and b) after alkaline hydrolysis

Figure 4.18 revealed a chromatogram showing peaks for the separated analytes from fenugreek non-hydrolysed and alkaline hydrolysed samples.

Fenugreek powder showed the presence of daidzein, genistein and secoisolariciresinol (in non hydrolysed and alkaline hydrolysed samples) and coumestrol (after alkaline hydrolysis).

During HPLC analysis of flaxseeds, we obtained one major peak at RT=13.55 from non-hydrolysed sample but it did not correspond to our standards' analytes. After alkaline hydrolysis, the flaxseeds showed the presence of daidzein, genistein and secoisolariciresinol. (Figure 4.19)

Non-hydrolysed sample of pomegranate confirmed the presence of daidzein while alkaline hydrolysis added the presence of genisteinmatairesinol as well (Figure 4.20).

Analysis of elephant foot yam confirmed the presence of genistein in non-hydrolysed sample, and genistein, daidzein, and matairesinol were detectable following alkaline hydrolysis (Figure 4.21)

All four foods, which we have analyzed, confirmed the presence of isoflavones (daidzein and genistein) and lignans (secoisolariciresinol/matairesinol). Coumestrolwas found only in fenugreek, rest all did not show its presence.

The results revealed and supportedthe findings that, the alkaline hydrolysis helps in better identification of phytoestrogen to compare theanalysis without hydrolysis with proposed method.Therefore the content of analytes received after alkaline hydrolysis was considered to calculate the total phytoestrogen content in foods.

The highest total isoflavone content was noted for elephant foot yam (172.4 µg/g) followed by fenugreek seeds (157 µg/g), pomegranate seeds (61.7 µg/g) and least by flaxseeds (32.6 µg/g) with the proposed method.

Fenugreek seeds showed the highest lignan content of 1893 µg/g followed by elephant foot yam (1216 µg/g), flaxseeds (1067 µg/g) and pomegranate (562µg/g).

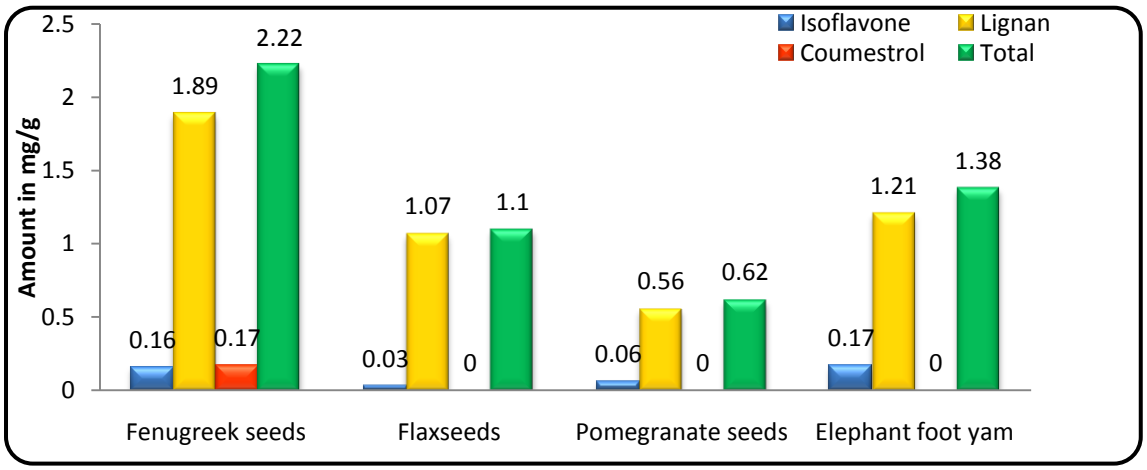


Figure 4.22: Estimated phytoestrogen components and content in all four food samples

Amongst all food samples fenugreek seeds ranked highest for total phytoestrogen content (2.22 mg/g), followed by elephant foot yam (1.38 mg/g), flaxseeds (1.1 mg/g) and the least was reported for pomegranate seeds (0.62 mg/g).

Several studies support the compounds having phytoestrogenic activity are present in fenugreek seeds, flaxseeds, elephant foot yam and pomegranate seeds, but as to our knowledge no studies have reported the similar phytoestrogen components we found in our study.

The efficacy of fenugreek seeds extract for estrogenic effect was studied *in vitro* by Sreeja and Anju (2010).The TLC chromatograph gave similar Rfvalues of 0.69 and 0.74 respectively for FCE (chloroform extract of fenugreek seeds) and 17-β estradiol standard indicating that phytoestrogenic compounds were present in FCE.Further they noted the proliferative effect of FCE relative to that of 17-β estradiol (10 nM, 100%) was expressed as relative proliferative effect (RPE). FCE (40 µg/ml to 320

μg/ml) significantly ($P< 0.05$) stimulated the proliferation of MCF-7 cells in a dose dependent manner as compared with that of unexposed control. At higher concentrations of 160 and 320 μg/ml the proliferative effect was almost similar to that of 10 nM 17-β estradiol (RPE = 91.74 ± 4.63 %). The ability of FCE to bind to ER was studied by competition binding studies using cytosol of MCF-7 cells. FCE inhibited the binding of labelled estradiol to ER. The degree of inhibition was found to be dependent on the concentrations of FCE and the labelled ligand. The authors concluded the ***potential estrogenic activities of chloroform extract of fenugreek seeds*** andfurther they mentioned the need to assess the physiological significance of fenugreek as an alternative to HRT and its importance as a dietary ingredient in the treatment of post menopausal health ailments in women.

Ahmed et al (2011) conducted a study to evaluate the effect of aqueous methanolic extract of flax seeds on serum estradiol, progesterone, kidney and liver functions and some serum biochemical metabolites in immature female rats. The reported aqueous methanol extract of flaxseeds increased serum estradiol, progesterone, total proteins, total cholesterol, ALT and AST activity, and decreased ovarian cholesterol levels, while it had no effect on kidney function in immature female rats.

Johnsson et al (2000) developed a method for analysis of secoisolariciresinoldiglucoside (SDG) in flaxseeds. They mentioned that base hydrolysis results into release of SDG from its polymer and acidification of extract prevent ionization of the carboxylic and phenolic groups. The study reported that secoisolariciresinoldiglycoside content was varied between 6.1 to 13.3 mg/g in whole flaxseeds.

Eliasson et al (2003) reported that SDG concentrations in twenty-seven flaxseed species ranged from 1.19 to 2.59% for (+)-SDG and from 0.22 to

0.5% (w/w) for its diastereoisomer, (-)-SDG. Moree and Rajesha (2011) mentioned that SDG is the main and abundant lignan in flaxseed; about 15 g of flaxseed contains approximately 13.6 mg of lignan.

S. De et al., (2010) did a phytochemical investigation and chromatographic evaluation of the different extracts of tuber of *Amorphophalluspaeoniifolius*. Their study confirmed the presence of alkaloids, steroids, fats & fixed oil, flavonoids, tannins, proteins and carbohydrates in tuber of *Amorphophalluspaeoniifolius*. But the type of steroids, flavonoids etc. were not studied in detail.

A pharmacological review on the elephant foot yam reveals that the plant is safer at its therapeutic dose of 250 mg/kg. It was found to bepotent analgesic, antiinflammatory, CNS depressant, anthelmintic, antibacterial, antifungal and cytotoxic agent. Itwas also seen that the benzodiazepine receptors may be involved for the CNS depressant activity. Thephytoconstituents which are present in the plant are mainly steroids and flavonoids which are responsible for theactions. More research is needed to isolate the constituents responsible for the biological actions. It was alsoobserved that no clinical trials have been done so far.

The traditional and ethnomedicinal literatures showed that, the elephant foot yam is very effective and safe plant for medicinal uses. Byusing the reverse pharmacological approaches in natural drug discovery a potent and safe drug can be investigatedfrom the plant for various chronic diseases like liver diseases, cancer, arthritis, and other inflammatory diseases. (Dey et al., 2012)

Bonzanini et al (2009) reported and quantified the lignansisolariciresinol, medioresinol, matairesinol, pinoresinol, secoisolariciresinol and syringaresinol for the first time in pomegranate (Punicagranatum L.) and in

its commercial preparation (juices) by means of GC–MS. The total lignan content in the different plant parts was estimated as follows: 36.1 ± 0.3 µg/g in seeds, 17.8 ± 0.2 µg/g in wood knots, 11.2 ± 0.2 µg/g in fruit pulp, 3.3 ± 0.1 µg/g in endocarp. Regarding the possible contribution of pomegranate-derived foods to dietary intake of lignans it must be noticed that in absence of a clear RDI/RDA for lignans, general nutritional suggestions rely on the epidemiologic correlations between intake and the onset of diseases. Recent surveys in representative European populations evidenced a mean total lignan daily intake of approximately 1 mg (Milder et al., 2005; Touillaud, Thiebaut, Fournier, Niravong, &Boutron-Ruault et al., 2007), which would be almost doubled by the assumption of less than 50 g of fresh pomegranate arils with seeds or homemade pomegranate squeeze or approximately 200 ml of pomegranate concentrated juice. In terms of nutraceutical value, it must be noticed that higher dietary intakes of lignans were associated with a reduction in the risk of postmenopausal breast cancers, in particular when the daily intake of lignans is above 1.5 mg (McCann et al., 2006; Touillaud et al., 2007).

Lansky et al (2000) reviewed the cross-cultural and ethnobotanical embodiments of pomegranate and noted that the seeds contain oil which contains not only the steroidal estrogen, estrone, in the highest concentration found in any botanical species, but also a full range of non-steroidal phytoestrogen including the comesten, coumestrol, and the isoflavones, genistein and daidzein. The findings of Choi et al (2005) are contradictory to these; they suggested there were no steroid estrogens including estrone, estradiol and testosterone in pomegranate seed, fruit juice and preparations.

In common, all four foods – fenugreek seeds, flaxseeds, and elephant foot yam and pomegranate seeds contain components with phytestogenic activity and have potential to combat menopausal illness. The reviews reported that daily consumption of 50 mg phytoestrogen may have beneficial role during menopausal transition.

Based on the quantification done with proposed method, amount of each food required to provide 50 mg phytoestrogen was calculated. The amount of fenugreek seeds and flaxseeds corresponds to 50 mg phytoestrogen were higher than commonly recommended doses. These may interfere or adversely affect the blood sugar level and lipid profile of women.

Hence in the current study, we supplemented the dry powder of elephant foot yam (tuber) and pomegranate seeds (provide 50 mg phytoestrogen) to perimenopausal women for 45 days. Phase 3 was planned to carry out these studies.

4.3 PHASE 3

Baseline Survey

The study population comprises women (n=150) from urban area of Vadodara district. An equal number of women (n=50) were distributed into three groups; EG1- Experimental group 1, EG2- Experimental group 2 and CG- Control group through blinding by a third person to avoid any biasness.

4.3.1 Socio demographic profile of the Subjects (N=150, EG1 – 50, EG2 – 50, CG – 50)

The mean age of EG1 was 40±3.3, EG2 was 40.7±3.1 and CG was 40.6±3.5. The distribution of women was same across three groups, there was no any significant difference amongst women of three groups for age (p=0.499).

Mean of monthly income was similar in all three study groups with an average of 17000 INR (p=0.153).

Their education profile revealed 47.9% of EG1 had completed their schooling up to 12, 39.6% had till 7^{th}, and only 10.4% had attained the graduation course; while majority of EG2 (53.1%) and CG (58.3%) had completed up to 7, and the number of women attaining graduation course for EG2 (8.2%) and CG (12.5%) was not differ much to the EG1 (10.4%).

Irrespective of study groups, majority of women were housewives (EG1 – 75%, EG2 – 83.7% and CG – 66.7%) and remaining was involved with some work.

Table 4.17: Socio-demographic profile of subjects (n=150)

	Experimental Group-1 (n=50)	**Experimental Group-2 (n=50)**	**Control Group (n=50)**
Age (Mean ± SD)	40±3.3	40.7±3.1	40.6±3.5
Age (Median ± SD)	40±3.3	41±3.1	40.5±3.5
Monthly Income	17251±4622	17010±5279	17204±4819
Education (n, %)			
Illiterate	1 (2.1)	1 (2)	0 (0)
Upto 7	19 (39.6)	26 (53.1)	28 (58.3)
Upto 12	23 (47.9)	18 (36.7)	14 (29.2)
>12 or Graduate	5 (10.4)	4 (8.2)	6 (12.5)
Profession (n, %)			
Housewife	36 (75)	41 (83.7)	32 (66.7)
Working	12 (25)	8 (16.3)	16 (33.3)
Number of children			
0 (No child)	0(0)	0 (0)	0 (0)
1	8 (16.7)	12 (24.5)	12 (25)
2	24 (50)	23 (46.9)	30 (62.5)
3	16 (33.3)	14 (28.6)	6 (12.5)
Number of pregnancy			
0 (No pregnancy)	0(0)	0 (0)	0 (0)
1-2	3 (6.3)	3 (6.1)	7 (14.6)
3-4	35 (73)	38 (77.6)	35 (72.9)
>4	10 (20.8)	8 (16.3)	6 (12.5)

Their parity profile revealed, half of women in each group (EG1 – 50%, EG2 – 46.9% and CG-62.5%) had 2 children and majority of women had undergone 3-4 pregnancies (EG1 – 73%, EG2 – 77.6% and CG – 72.9%), though there were few no. of women who had undergone pregnancies for more than 4 times.

The distribution of age, monthly income, parity number, and education level found similar in all study groups (experimental- EG1 and EG2, control – CG).

4.3.2 Effect of Intervention on Anthropometric indicators

Anthropometric measurements were carried out before and after supplementation for weight (wt), waist circumference (WC), and hip circumference (HC) and height (ht) measurement was done only at baseline for women in all three groups (EG1, EG2 and CG). Using these measurements as yardsticks, body mass index (BMI) and waist to hip ratio (WHR) were calculated to know the nutritional status of women.

Table 4.18 shows the anthropometric measurements; mean of weight, height, waist circumference, hip circumference and calculated BMI and WHR for all three study groups. At baseline, there were no major differences observed in mean weight ($p=0.083$), height ($p=0.67$), WC ($p=0.121$), and HC ($p=0.07$) amongst women between three groups.

The nutritional status of women based on their BMI revealed: in EG1 - 19 (39.6%) women were normal, 25 (52.1%) were overweight and 4 (8.3%) were obese, similarly in EG2 19 (38.8%) were normal, 29 (59.2%) were overweight and 1 (2%) were obese; and in control group 18 (37.5%) were normal, 27 (56.2%) were overweight and 3(6.2%) were obese at baseline (Table 4.19).

Table 4.18: Changes in anthropometric indicators – before and after intervention in all three groups (EG1, EG2 and CG)

	EG1 (n=48)		EG2 (n=49)		CG (n=48)	
Indicator	Before (Mean±SD)	After (Mean±SD)	Before (Mean±SD)	After (Mean±SD)	Before (Mean±SD)	After (Mean±SD)
Weight (kg)	62±7.4	60.6±6.9↓	61.3±7.5	60.2±7.4↓	63.2±7.4	63.1±7.5↓
Height (cm)	155±5.1	-	155.1±4.7	-	156.9±4.1	-
BMI (kg/m^2)	25.9±3.4	25.3±3.2↓	25.5±2.8	24.8±3.2↓	25.7±3	25.7±3.04
WC(cm)	89.67±4.7	88.65±5↓	90.80±4.5	90.12±4.4↓	90.5±4.5	90.06±4.8
HC(cm)	104.7±9	104.2±9↓	103.8±7.3	103.3±7.2↓	102.2±4.7	102.4±6.5
WHR	0.86±0.05	0.85±0.05↓	0.88±0.04	0.87±0.05↓	0.88±0.05	0.88±0.04

Table 4.19: Nutritional status of women based on their BMI – before and after intervention in all three groups (EG1, EG2 and CG)

Nutritional Status	EG1 (n=48)		EG2 (n=49)		CG (n=48)	
	Before N (%)	After N (%)	Before N (%)	After N (%)	Before N (%)	After N (%)
Underweight	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)
Normal	19 (39.6)	24 (50) ↑	19 (38.8)	22 (44.9) ↑	18 (37.5)	20 (42.6) ↑
Overweight	25 (52.1)	20 (41.7) ↓	29 (59.2)	25 (51) ↓	27 (56.2)	24 (51.1) ↓
Obese	4 (8.3)	4 (8.3)	1 (2)	1 (2)	3 (6.2)	3 (6.4)

Table 4.20: Correlation and t-statistics for anthropometric indicators in all three groups (EG1, EG2 and CG)

	EG1 (n=48)			EG2 (n=49)			CG (n=48)		
Indicator	**Correlation (Significance)**	**t-value**	**Significance (2-tailed)**	**Correlation (Significance)**	**t-value**	**Significance (2-tailed)**	**Correlation (Significance)**	**t-value**	**Significance (2-tailed)**
Weight (kg)	0.976 (0.000)	5.89	0.000***	0.992 (0.000)	8.30	0.000***	0.994 (0.000)	0.52	0.606
BMI (kg/m^2)	0.981 (0.000)	6.01	0.000***	0.886 (0.000)	3.18	0.003**	0.994 (0.000)	0.56	0.572
WC(cm)	0.840 (0.000)	2.55	0.014**	0.979 (0.000)	5.11	0.000***	0.989 (0.000)	3.94	0.000***
HC(cm)	0.940 (0.000)	1.19	0.238	0.994 (0.000)	4.49	0.000***	0.870 (0.000)	-0.52	0.605
WHR	0.877 (0.000)	0.32	0.752	0.981 (0.000)	2.47	0.017*	0.900 (0.000)	1.69	0.098

Significantly different at p<0.05, p<0.01**, p<0.001**

Mean±SD for weight in EG1, EG2 and CG were 62±7.4, 61.3±7.5, and 63.2±7.4 respectively before intervention; which were reduced significantly to 60.6±6.9 ($p<0.001$) in EG1, 60.2±7.4 ($p<0.001$) in EG2 and non-significantly to 63.1±7.5 ($p=0.6$) in CG (Table 4.18).

Similarly for BMI, EG1 showed a significant reduction from 25.9±3.4 to 25.3±3.2 ($p<0.001$) and EG2 from 25.5±2.8 to 24.8±3.2 ($p<0.01$). No change was observed for BMI in control group.

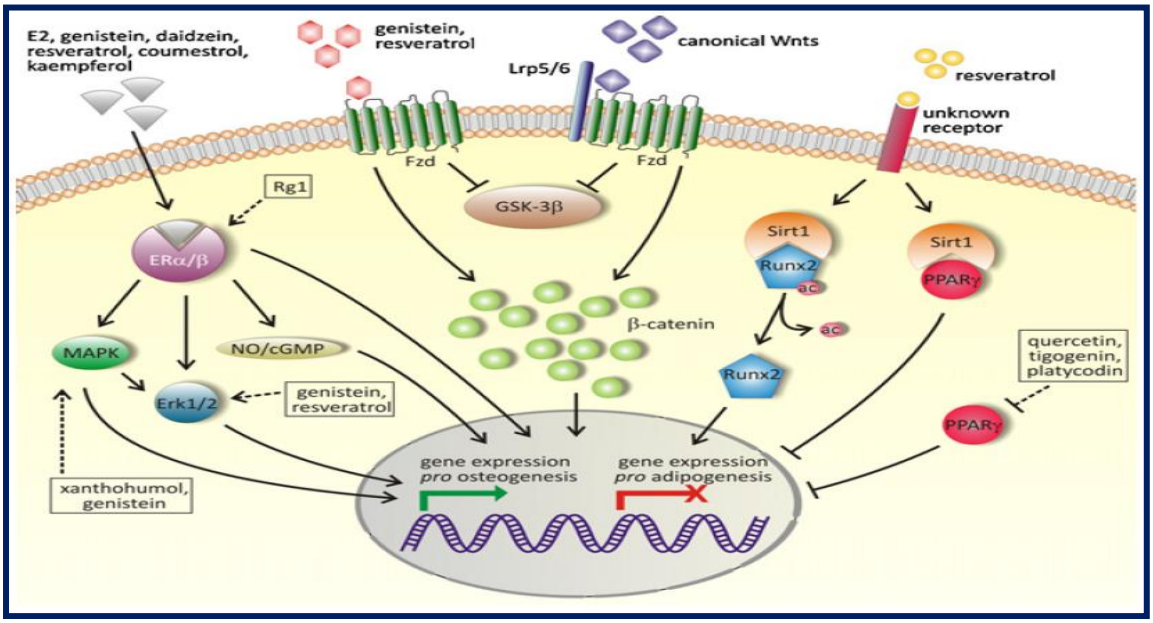
Waist circumference was significantly reduced in all three groups; in EG1 – from 89.67±4.7 to 88.65±5 ($p<0.01$), in EG2 – from 90.80±4.5 to 90.12±4.4 ($p<0.001$) and in CG – from 90.5±4.5 to 90.06±4.8 ($p<0.001$).

For hip circumference and WHR, a reduction was seen in both experimental groups EG1 and EG2 but significant reduction was seen in EG2 only; where HC was reduced from 103.8±7.3 to 103.3±7.2 ($p<0.001$) and WHR from 0.88±0.04 to 0.87±0.05 ($p<0.05$).

The possible mechanism behind a reduction in weight amongst experimental groups (EG1 and EG2) is, phytoestrogen have been shown to activate Wnt and Sirt1 signalling pathways in MSCs which leads to the activation of osteogenic gene transcription whereas genes promoting adipogenic differentiation are repressed.(Scilling et al., 2013)

In addition, daidzein has been proposed to prevent the differentiation of MSCs into mature adipocytes by the stimulation of lipolysis from adipocytes, i.e. via increased glycerol release from differentiated adipocytes. According to Dang et.al., (2002) and Okazaki et.al.,(2002), Estrogen signalling is capable to inhibit the adipogenic differentiation in mesenchymal stem cells (MSCs). Due to the structural similarities with Estradiol, phytoestrogen can bind to estrogen receptors and they possess estrogen like activity as they alleviate postmenopausal complaints, increase

bone formation and repress adipose tissue similar to E2. (Song et al., 2007; Heim et al., 2004)



(Source: Schilling et al., 2013)

Figure 4.23: Role of Wnt and Sirt1 signalling pathways in repressing adipognesis

Amongst control group, such significant reduction was not observed for weight and body mass index. The marginal reduction observed for waist circumference was might be due to the stretching exercise, which indicated that translocation of fat was started in women. Though the efforts were not sufficient to burn the fat or calories which could help in weight reduction.

Though we have not studied the effect of phytoestrogen on lipid profiles, several studies have been reported the phytoestrogen supplementation play a positive role in insulin resistance, glycemic index and serum lipoproteins in postmenopausal women with type 2 diabetes and help in reduction of cardiovascular risks. (Jaygopal et al., 2002)

Merz et al (2006) suggested that higher blood phytoestrogen daidzein levels are associated with beneficial blood lipoprotein levels in women with cardiac risk factors undergoing evaluation for suspected myocardial ischemia. Instead, in our study we have focus on abdominal obesity, and study findings supports the phytoestrogen and lifestyle approach help to reduce abdominal obesity, thereby indirectly reduce the risks of NCDs.

4.3.3 Effect of Supplementation on Menopause related symptoms

After collection of baseline data, few subjects (n=5) were dropped the study in between study period (details are provided in methodology, page no. 161) and hence total number of subjects was differ at completion of the study. For the analysis of results, the subjects who had completed the study in a correct manner were considered.

Symptoms for MRS:

EG1:

In EG1 (Table 4.21), the women reported the physical and mental exhaustion (91.7%) was the most prevalent (73.6%), followed by anxiety (89.6%), pain in hands or legs (85.4%), mood swings (85.4%), irritability (85.4%), dryness of vagina (85.4%) and sleep disturbances (81.2%), hot flashes (81.2%). The other symptoms like heart discomfort (72.9%), sexual problems (70.8%), and bladder problems (70.8%) were also reported by majority of women.

Table 4.21: Percent prevalence of menopausal symptoms – At baseline

Symptoms	EG1 (n=48)		EG2 (n=49)		CG (n=48)	
	Yes	No	Yes	No	Yes	No
Hot flashes	81.2	18.8	85.7	14.3	83.3	16.7
Heart Discomfort	72.9	27.1	53.1	46.9	64.6	35.4
Sleep problems	81.2	18.8	91.8	8.2	95.8	4.2
Mood swings	85.4	14.6	65.3	34.7	62.5	37.5
Irritability	85.4	14.6	79.6	20.4	70.8	29.2
Anxiety	89.6	10.4	95.9	4.1	89.6	10.4
Physical and Mental Exhaustion	91.7	8.3	91.8	8.2	91.7	8.3
Sexual problem	70.8	29.2	51	49	72.9	27.1
Bladder problems	70.8	29.2	71.4	28.6	72.9	27.1
Dryness of vagina	85.4	14.6	85.7	14.3	72.9	27.1
Pain in hands and legs	85.4	14.6	95.9	4.1	95.8	4.2
Swelling	25	75	26.5	73.5	16.7	83.3
Weight fluctuation	25	75	16.3	83.7	8.3	91.7
Hair loss	68.7	13.3	83.7	16.3	87.5	12.5
Constipation	18.7	81.3	16.3	83.7	14.6	85.4
Visual Problem	37.5	62.5	26.5	73.5	8.3	91.7
Nails Cracking	39.6	60.4	6.1	93.9	6.2	93.8

EG2:

In EG2 (Table 4.21), the women reported the pain in hands or legs (95.9%) and anxiety (95.9%) were the most prevalent, followed by physical and mental exhaustion, (91.8%), sleep disturbances (91.8%), dryness of vagina (85.7%) , hot flashes (85.7%). The other symptoms like irritability (79.6%), bladder problems (71.4%), and mood swings (65.3%) were also reported by majority of women, while heart discomfort (53.1%) and sexual problems (51%) were reported by half of the women.

CG:

In CG (Table 4.21), pain in hands or legs (95.8%) and sleep disturbances (95.8%) were the most prevalent, followed by physical and mental exhaustion, (91.7%), anxiety (89.6%), hot flashes (83.3%). The urogenital symptoms like dryness of vagina, bladder problems and sexual problems were reported by 72.9%, followed by irritability (70.8%). While heart discomfort (64.6%), and mood swings (62.5) were reported by more than half of the women.

Other Menopause related symptoms:

EG1:

Amongst other symptoms related with menopause, hair loss was reported by 68.7% women, nails cracking by 39.6%, visual problem by 37.5%, swelling by 25%, weight fluctuation by 25%, and only 18.7% women were reported constipation.

EG2:

Approx eighty four percent complained for hair loss, 26.5%for swelling and visual problem, 16.3% for weight fluctuation and constipation and only 6.1% women for nails cracking.

CG:

Hair loss was reported by 85.7% women, swelling by 16.7%. Constipation by 14.6%, weight fluctuation and visual problem by 8.3% and only 6.2% women were reported nails cracking.

After intervention

Symptoms for MRS:

The women supplemented with yam and pomegranate *showed a reduction in prevalence of all 11 symptoms for MRS*. The women in control group also reported reduction in few of the symptoms (Table 4.22).

The percent improvement in symptoms experienced and its significance level was depicted in Table 4.23.

Among the women with phytoestrogen supplementation: EG1 showed greater improvement for 56% in bladder problems, 49% in hot flashes, 46% mood swings, sleep problems. Women in EG2 reported 82.8% improvement in bladder problems, 59.5% in hot flashes, 38.5% in heart discomfort, 37.5% in mood swings, 35.6% sleep problems.

The women of control group (CG) who were not provided the phytoestrogen, but nutrition and physical health education was imparted to them, showed a significant improvement for 19.6% in sleep problems, 17.5 % in bladder problems, 17.1% in bladder problems, 14.3% in sexual problems, 9% in irritability and anxiety. It is important to note that experience of few symptoms like heart discomfort and mood swings were increased from baseline in women of this group.

The results were indicative of mimicking action of phytoestrogen to estradiol play a role to ameliorate the suffering of menopausal symptoms. Other alternatives may help to lighten the scenario, but not to a great extent, as in case with control group.

Dr. Debra Anderson, a senior lecturer in Women's Health had developed the Women's wellness Program (2003) which was a 12-week lifestyle intervention program. Total 120 women ranging in age from 50 to 65 were provided with a book (The Menopause made simple Program) about lifestyle tips and exercise published by study authors Allen and Unwin and encouraged to increase dietary phytoestrogens through eating more soy-based foods and grains, raise calcium intake and drink eight glasses of water daily. The study findings reported a significant reduction not only in menopausal symptoms such as hot flashes and palpitations, feeling of depression, fatigue and lack of motivation by women, but also in body fat, particularly abdominal fat, and blood pressure. (www.whfoods.com/genpage.php?tname=disease&dbid=8)

Table 4.22: Percent prevalence of menopausal symptoms – after intervention

Symptoms	EG1 (n=48)		EG2 (n=49)		CG (n=48)	
	Yes	No	Yes	No	Yes	No
Hot flashes	37.5↓	62.5	34.7↓	65.3	68.7↓	31.3
Heart Discomfort	56.2↓	43.8	32.7↓	67.3	**66.7**↑	33.3
Sleep problems	50.0↓	50	59.2↓	40.8	77.1	22.9
Mood swings	45.8↓	54.2	40.8↓	59.2	**68.8**↑	31.3
Irritability	52.1↓	47.9	49.0↓	51	64.6↓	35.4
Anxiety	64.6↓	35.4	77.6↓	22.4	81.2↓	18.8
Physical and Mental Exhaustion	72.9↓	27.1	69.4↓	30.6	91.7	8.3
Sexual problem	56.2↓	43.8	32.7↓	67.3	62.5↓	37.5
Bladder problems	31.3↓	68.8	12.2↓	87.8	60.4↓	39.6
Dryness of vagina	56.2↓	43.8	65.3↓	34.7	70.8↓	29.2
Pain in hands and legs	60.4↓	39.6	77.6↓	22.4	91.7↓	8.3
Swelling	22.9↓	77.1	24.5↓	75.5	16.7	83.3
Weight fluctuation	22.9↓	77.1	14.3↓	85.7	6.02↓	93.8
Hair loss	68.7	31.3	83.7	16.3	87.5	12.5
Constipation	18.7	81.3	20.4	79.6	14.6	85.4
Visual Problem	37.5	62.5	26.9	73.1	8.3	91.7
Nails Cracking	37.5↓	62.5	6.1	93.9	6.2	93.8

Table 4.23: Percent improvement in menopausal symptoms – after intervention

Symptoms	EG1 (n=48)		EG2 (n=49)		CG (n=48)	
	%	p-value	%	p-value	%	p-value
Hot flashes	48.7	<0.001***	59.5	<0.001***	17.5	<0.001***
Heart Discomfort	22.8	0.003**	38.5	0.004**	-	0.405$^{(NS)}$
Sleep problems	38.5	<0.001***	35.6	<0.001***	19.6	<0.001***
Mood swings	46.3	<0.001***	37.5	0.001**	-	0.220$^{(NS)}$
Irritability	39.0	<0.001***	38.5	<0.001***	8.8	0.242$^{(NS)}$
Anxiety	27.9	<0.001***	19.2	0.001**	9.3	0.001**
Physical and Mental Exhaustion	20.5	<0.001***	24.4	<0.001***	0	0.317$^{(NS)}$
Sexual problem	20.6	0.005**	36	0.003**	14.3	0.159$^{(NS)}$
Bladder problems	55.9	<0.001***	82.8	<0.001***	17.1	0.021*
Dryness of vagina	34.2	<0.001***	23.8	0.001**	2.9	0.405$^{(NS)}$
Pain in hands and legs	29.3	<0.001***	19.2	<0.001***	4.4	0.008**

(Contd.)

Symptoms	EG1 (n=48)		EG2 (n=49)		CG (n=48)	
	%	p-value	%	p-value	%	p-value
Swelling	8.33	0.083$^{(NS)}$	7.69	0.102$^{(NS)}$	0	0.317$^{(NS)}$
Weight fluctuation	8.33	0.157$^{(NS)}$	12.5	0.317$^{(NS)}$	25	0.083$^{(NS)}$
Hair loss	0	1.000$^{(NS)}$	0	0.03*	0	0.046$^{(NS)}$
Constipation	0	1.000$^{(NS)}$	-	0.157$^{(NS)}$	0	0.038*
Visual Problem	0	1.000$^{(NS)}$	0	1.000$^{(NS)}$	0	1.000$^{(NS)}$
Nails Cracking	5.2	0.157$^{(NS)}$	0	1.000$^{(NS)}$	0	1.000$^{(NS)}$

Effect of Intervention on MRS

For assessment of the menopausal symptoms, menopausal rating scale was established as a standardized instrument due to its reliability, the short format encompassing all the associated symptoms and the simple scoring scheme. (Kakkar et al, 2007) According to MRS, the symptoms were grouped into three dimensions: Psychological, Somato-vegetative and Urogenital.

In the present study we oserved the changes in MRS in experimental groups (EG1- Yam supplementation, EG2-Pomegranate supplementation) and in control group (CG) before and after intervention of phytoestrogen supplementation and NHE.

Table 4.24 depicts the Mean MRS value for before and after supplementation for all three groups (EG1, EG2 and CG) along with the mean values for three dimensions of MRS i.e., Psychological, Somato-vegetative and Urogenital. The mean±SD of MRS in EG1 and EG2 were 11.9±2.5 and 11.1±1.8 at baseline, which were reduced to 6.3±3.8 and 6.0±2.2 respectively after supplementation. A reduction in mean±SD of MRS was also observed in CG group where 11.2±1.5 was reduced to 9.0±1.7. The mean value showed a marked reduction for all three dimensions in all three groups (EG1, EG2, and CG) as well.

Before and after supplementation, women of each group (EG1, EG2 and CG) observed a significant improvement in an individual MRS score ($p<0.001$) (Figure 4.24).

Table 4.24: Mean of MRS along with Mean of its three subscales (P, S & U) in all study groups (EG1, EG2 and CG) – before and after intervention

	EG-1 (Mean±SD)		EG-2 (Mean±SD)		CG (Mean±SD)	
	Before	**After**	**Before**	**After**	**Before**	**After**
Psychological Sub-score (P)	4.8±1.3	2.5±1.5	4.4±1.0	2.2±1.1	4.2±1.5	3.6±1.0
Somatic Sub-score (S)	4.6±1.4	2.3±1.7	4.4±1.3	2.2±1.1	4.5±1.1	3.3±0.9
Urogenital sub-score (U)	2.5±1.0	1.5±1.2	2.3±0.8	1.1±0.8	2.6±0.9	2.1±1.1
MRS	11.9±2.5	6.3±3.8	11.1±1.8	6.0±2.2	11.2±1.5	9.0±1.7

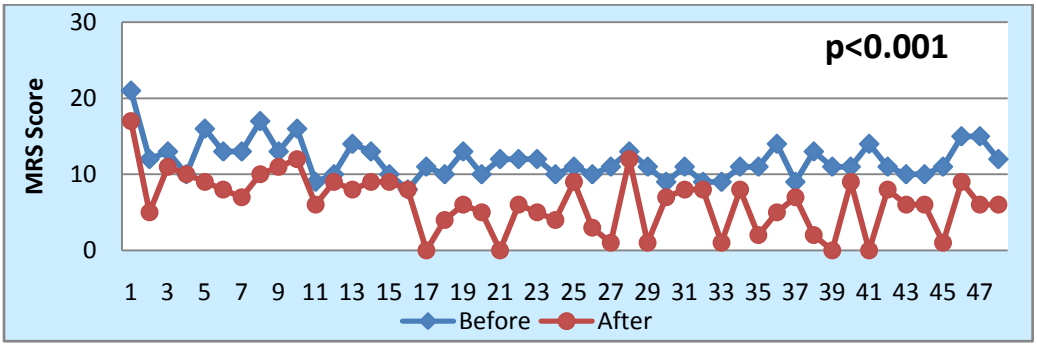
Figure 4.24: Effect of Intervention on MRS

(a) Effect of Yam Supplementation in EG1

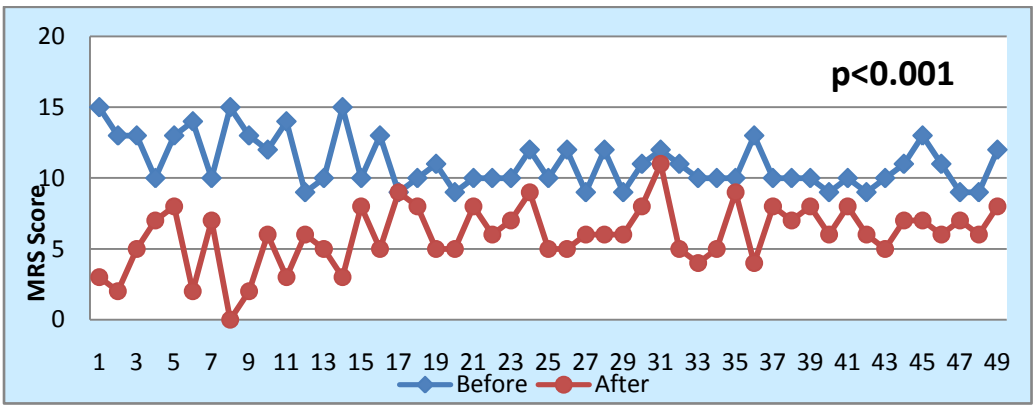
(b) Effect of Pomegranate Supplementation in EG2

(c) Effect of NHE and exercise in CG

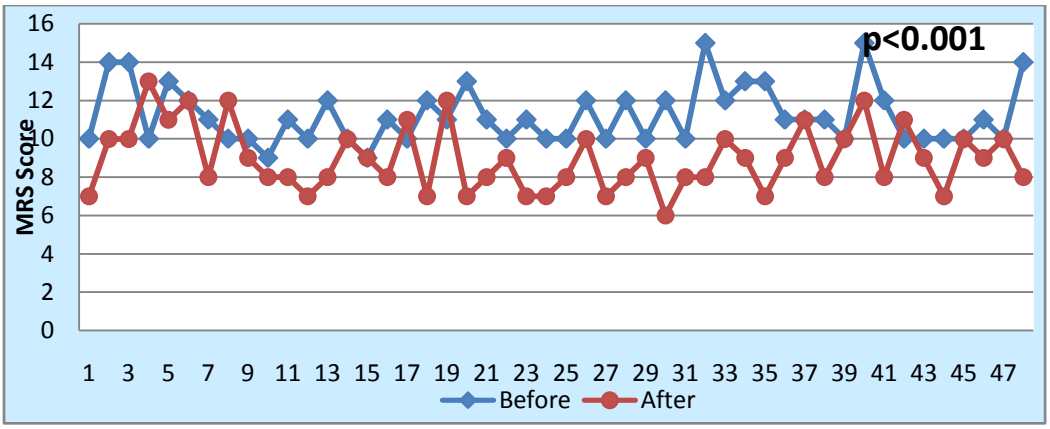
(a)



(b)



(c)



The overall reduction in MRS and all three dimensions support a hypothesis that alternative therapies are useful for symptomatic relief during menopausal transition; the reduction in experimental groups (EG1 and EG2) revealed that phytoestrogen supplementation and laughing and stretching exercise helped in symptomatic relief during menopausal transition.

These findings showed statistically significance on post-hoc analysis using Independent sample-Kruskal-Wallis test. There was no significant difference in distribution of MRS at baseline amongst all three groups, while after supplementation there was significant difference in distribution of MRS ($p<0.001$) (Figure 4.25). Between the groups analysis revealed a significant difference in mean MRS between EG1 - CG ($p<0.001$) and EG2 – CG ($p<0.001$) while no significant difference between EG1-EG2 ($p=0.508$).

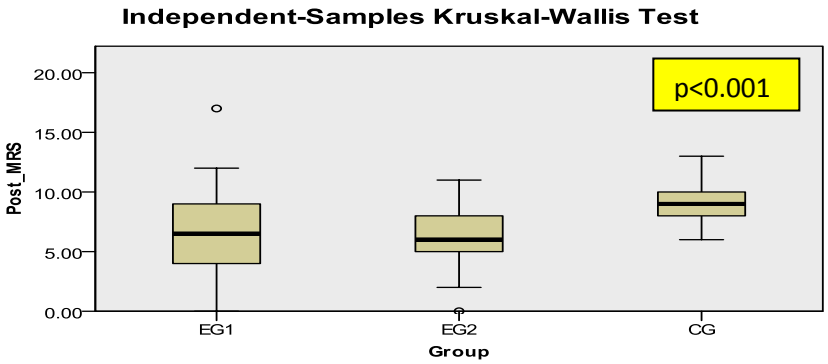


Figure 4.25: Post intervention changes in distribution of MRS – amongst experimental (EG1 & EG2) and control (CG) groups

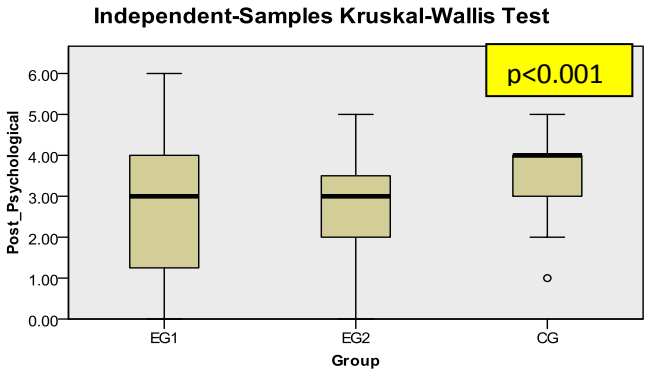


Figure 4.26: Post intervention changes in distribution of P (Psychological) score – amongst experimental (EG1 & EG2) and control (CG) groups

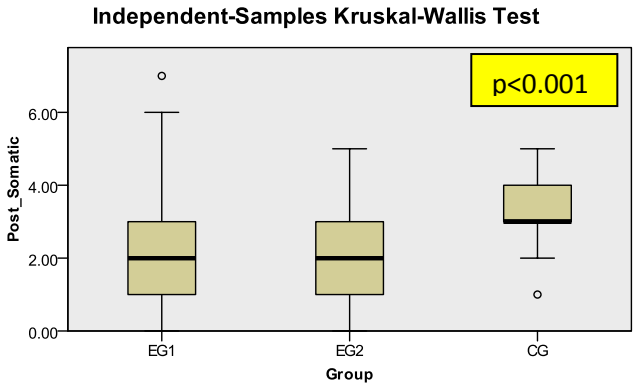


Figure 4.27: Post intervention changes in distribution of S (Somato-vegetative) score – amongst experimental (EG1 & EG2) and control (CG) groups

There was no significant difference in distribution of P score (Psychological Score) at baseline amongst all three groups (p=0.056), while after supplementation there was significant difference in mean P score (p<0.001). Between the groups analysis revealed a significant difference in mean P score between EG1 - CG (p=0.001) and EG2 – CG (p=0.003) while no significant difference between EG1-EG2 (p=1.000).

Similarly, there was no significant difference in distribution of S (Somato-vegetative) score and U (Urogenital) score at baseline amongst all three groups , while after supplementation there was significant difference in their distribution ($p<0.001$). Between the groups analysis revealed a significant difference in mean S score between EG1 – CG and EG2 – CG ($p<0.001$) and no significant difference between EG1-EG2 ($p=1.000$) (Figure 4.27); similarly for mean U score a significant difference between EG1 – CG ($p<0.001$) and EG2 – CG ($p=0.033$) and no significant difference between EG1-EG2 ($p=0.210$) (Figure 4.28).

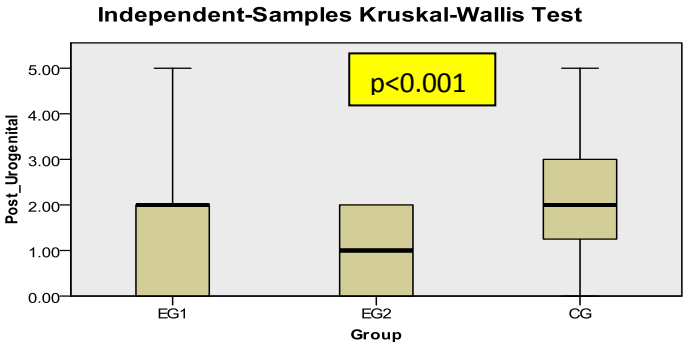


Figure 4.28: Post intervention changes indistribution in U (Urogenital) score – amongst experimental (EG1 & EG2) and control (CG) groups

Mittal et al., (2011) conducted a study double-blind placebo-controlled trail to evaluate the effect of isoflavones on thyroid function, menopausal symptoms, serum FSH and estradiol levels in 43 oophorectomised women from Chandigarh, India. The study findings revealed after 12 week of soy isoflavones (75mg/day) intervention, the Menopause Symptom Score was reduced from 12.47±8.15 to 9±5.14 in isoflavone supplemented group and 11.53±6.18 to 11±6.96 in placebo group. The mean change in

Psychological, Somatovegetative and Urogenital sub scores were -2.29±3.93, -0.47±2.83 and -0.71±1.16 respectively in Isoflavone supplemented group. Though while comparing with the placebo group, a significant improvement was seen only for the urogenital symptoms.

Davis SR (2001) had mentioned that Women experiencing mild menopausal symptoms may gain relief by dietary modification and lifestyle changes, such as reducing smoking and consumption of caffeine and alcohol, stress management, and increased exercise.

Shakila et al., (2015) conducted a study to assess women's awareness and symptoms in menopause of women in sri Lanka and they suggested the exercise program for peri and post-menopausal women should include endurance exercise (aerobic), strength exercise, and balance exercise. Out of these aerobics, weight bearing, and resistance exercises are all effective in increasing the bone mineral density of the spine in postmenopausal women (Bonaiuti D 2002). An effective exercise prescription may be resistance and weight bearing exercise three days a week (on alternate days). Care should be taken to do the exercise for all the muscle groups by rotation preferably with a trainer. Brisk walking at the speed of five to six kilometers per hour is a must for all women but especially it is very good for menopause women a lot. Cycling, treadmill, gardening or dancing may be done on the remaining days of the week. Warming up beforehand can help to reduce exercise related injuries and pain following exercise. One should aim for two hours and 30 minutes of moderate aerobic activity each week. Other deep breathing, yoga, and stretching exercises can help to manage the stress of life and menopause-related symptoms

Similarly in the present study we also observed a significant reduction in mean of Psychological, Somatovegetative and Urogenital sub-scores in

experimental (EG1 and EG2) and control groups (CG) after intervention. With our study population (control group), we recommend activities like yoga, stretching and laughing exercise at least thrice a week.

Laughing leads to the release of endorphins, which carries messages of attachment and bonding (the scientific terms for love), and to stimulate feelings of caring and forgiveness in addition to acting as a natural painkiller.

Endorphins create a positive state of mind and boost optimism, self confidence and feelings of self-worth. This would prove beneficial to our population.

While evaluating between experimental and control groups in present study, we also noted a significant difference for improvement in MRS between EG1-CG and EG2-CG.

This suggested though we observed a relief in MRS in control group, the women in experimental groups had greater relief in MRS, where phytoestrogen could have play a role. This significant difference supports that life style approaches along with phytoestrogen supplementation help better in ameliorating menopausal symptoms.

4.3.4 Effect of Intervention on Biochemical parameters

Table 4.25:Mean±SD of selected biochemical parameters in all study groups (EG1, EG2 and CG) - before and after intervention

Parameters	EG1 (n=48)		EG2 (n=49)		CG (n=48)	
	Before (Mean+SD)	After (Mean+SD)	Before (Mean+SD)	After (Mean+SD)	Before (Mean+SD)	After (Mean+SD)
Hb(g/dl)	10.38±1.98	11.30±1.99	9.99±1.93	10.66±1.91	10.01±1.89	10.33±2.14
FSH (mIU/ml)	87.55±29.44	51.74±32.22	84.25±24.30	64.18±30.26	71.73±33.50	54.86±31.10
LH(mIU/ml)	62.38±24.49	36.48±33.25	57.82±29.64	34.09±25.07	41.88±30.50	25.47±18.04
Estradiol(pg/ml)	89.76±46.64	130.24±39.23	82.73±34.80	132.35±40.98	120.34±46.12	101.97±39.86
T3(ng/dl)	109.33±17.58	112.52±13.76	111.76±17.26	111.76±13.3	112.35±20.0	111.67±16.10
T4(µg/dl)	8.42±1.99	8.9±2.13	8.24±2.13	8.87±2.25	8.52±1.99	8.72±2.14
TSH(µIU/ml)	3.79±2.38	3.86±2.08	3.51±2.68	3.76±2.43	3.66±1.99	3.79±1.86

Table 4.26: Correlation and t-statistics for biochemical parameters in all study groups (EG1, EG2 and CG)

	EG1 (n=48)		EG2 (n=49)		CG (n=48)	
Indicator	Correlation (Significance)	Significance (2-tailed)	Correlation (Significance)	Significance (2-tailed)	Correlation (Significance)	Significance (2-tailed)
Hb(g/dl)	0.805 (0.000)	0.000***	0.282 (0.050)	0.048*	-0.043 (0.773)	0.449
FSH (mIU/ml)	0.133(0.368)	0.000***	0.121(0.406)	0.000***	0.497 (0.000)	0.001**
LH(mIU/ml)	0.109 (0.461)	0.000***	0.378 (0.007)	0.000***	0.466 (0.001)	0.000***
Estradiol (pg/ml)	0.478 (0.001)	0.000***	0.120 (0.422)	0.000***	-0.128 (0.385)	0.055
T3(ng/dl)	0.468 (0.001)	0.187	0.378 (0.007)	1.000	0.256 (0.080)	0.831
T4(µg/dl)	0.587 (0.000)	0.087	0.240 (0.096)	0.107	0.402 (0.005)	0.541
TSH(µIU/ml)	0.969 (0.000)	0.390	0.958 (0.000)	0.032**	0.959 (0.000)	0.099

Significantly different at p<0.05, p<0.01**, p<0.001**

The effect of phytoestrogen supplementation and NHE intervention was also assessed on biochemical parameters i.e. Hb, FSH, LH, Estradiol, T3, T4 and TSH (Table 4.25, 4.26).

In experimental groups EG1 and EG2, mean Hb values were 10.38±1.98 and 9.99±1.93 before supplementation, and increased to 11.30±1.99 and 10.66±1.91 respectively after supplementation. These changes were statistically significant ($p<0.001$ and $p<0.01$). In control group the mean Hb was 10.01±1.89 which non-significantly increased to 10.33±2.14.

The serum gonadotropins, FSH and LH had shown a significant reduction amongst all study groups (EG1, EG2 and CG).

The mean±SD of FSH in EG1 and EG2 were 87.55±29.44 and 84.25±24.30 at baseline, which were reduced to 51.74±32.22 and 64.18±30.26 respectively after supplementation ($p<0.001$). A reduction in mean±SD of FSH was also observed in CG group where 71.73±33.50 was reduced to 54.86±31.10 ($p<0.01$).

The mean±SD of LH in EG1 and EG2 were 62.38±24.49 and 57.82±29.64 at baseline, which were reduced to 36.48±33.25 and 34.09±25.07 respectively after supplementation ($p<0.001$). A reduction in mean±SD of LH was also observed in CG group where 41.88±30.50 was reduced to 25.47±18.04 ($p<0.001$).

In contrary to serum gonadotropins, serum estradiol level had shown a significant increase in the groups supplemented with phytoestrogen rich foods (EG1 and EG2) while in the control group such improvement in serum estradiol was not seen.

Before intervention the mean±SD of serum estradiol were 89.76±46.64 and 82.73±34.80 in EG1 and EG2 which increased to 130.24±39.23 and 132.35±40.98 respectively ($p<0.001$).

There have been reports of both reduced and increased serum E, concentrations in premenopausal women and reduced serum E_2 concentrations in postmenopausal women after soy consumption. (Xu et al., 1997)

A meta-analysis of randomized trials evaluating the effect of soy food or purified isoflavones on reproductive hormone levels or menstrual cycle characteristics found that, among premenopausal women, soy food or isoflavone supplementation resulted in significantly lower circulating FSH and LH levels (about 20% lower). (Hooper et al., 2009)

Kurzer MS (2002) reviewed seven studies with intakes of 32-200 mg of isoflavones/d and observed that after soy intake there was a decreased in mid cycle gonadotropins, trends for increased cycle length, and lower estradiol, progesterone, and serum hormone binding globulin.

A large review of 47 studies (11 pre-, 35 post-, and 1 perimenopausal women) conducted by Hooper at al., (2009) showed no differences in post menopausal women, whereas studies involving premenopausal women showed no effect on estradiol, estrone, or SHBG but did show decreased FSH and LH along with increased cycle length.

Data in human are inconsistent for the effect of phytoestrogen supplementation at hormones level; in the present study we observed a decline in serum FSH and LH level in perimenopausal women. Earlier studies observed the similar results in premenopause women but no clear

evidence for perimenopause. We also observed an improvement in serum estradiol level, which was not reported earlier.

For thyroid hormone profile (T3, T4, and TSH), the intervention did not show any significant changes from baseline values in all study groups, except the mean TSH was significantly increased in EG2 (from 3.51±2.68 to 3.76±2.43).

There are no such studies available where the effect of phytoestrogen consumption was seen amongst women in perimenopause. Most of the research studies were emphasized and discuss the use of phytoestrogen in postmenopausal women.

4.3.5 Knowledge and Perceptions related to Menopausal health

Women during the menopause period experience certain physical and psychological changes and face various problems such as urogenital, psychological–social, cardiovascular and neurological problems, etc. These problems not only cause great distress and disability for the person but also impose a lot of pressure on the limited resources of the countries' health care system. Familiarity with these changes and understanding their reasons are essential in the life of all women, and helps them enter this stage of their life with adequate knowledge and a positive attitude.

In the present study, the subjects were assessed for their knowledge and perceptions on menopause and related issues. The study findings revealed there was no much difference in the knowledge amongst women in all study groups (EG1, EG2 & CG).

Majority of women had heard about menopause (EG1-68.8%, EG2-83.7%, CG-81.3%), half of them had heard about Iodised salt (EG1-56.3%, EG2-77.6%, CG-62.5%) and few about calcium (EG1-35.4%,

EG2-38.8%, CG-37.5%). They did not know about HRT, phytoestrogen, relation of thyroid & menopause and bone health at baseline.

After an intervention of 45 days, their knowledge improved a lot. The entire study participants were able to understand about menopause, HRT, phytoestrogen, calcium, relation of menopause with thyroid and bone health. The details were given in figure 4.29 and their statistical significance was depicted in table 4.27.

Their perceptions regarding menopausal symptoms, symptoms of thyroid, importance of iodized salt and calcium were also improved significantly after an intervention. But the improvement was similar for all study groups, there was no any significant difference for these amongst experimental and control groups (EG1, EG2 and CG) (Table 4.28 to table 4.31, figure 4.29).

At baseline, majority of women did not answer anything about menopausal symptoms and very few replied but they reported aging, impaired vision, and abdominal pain as menopausal symptoms. After study period, majority were able to report hot flashes, sleep disturbances, mood swings, and bladder problems etc as menopausal symptoms.

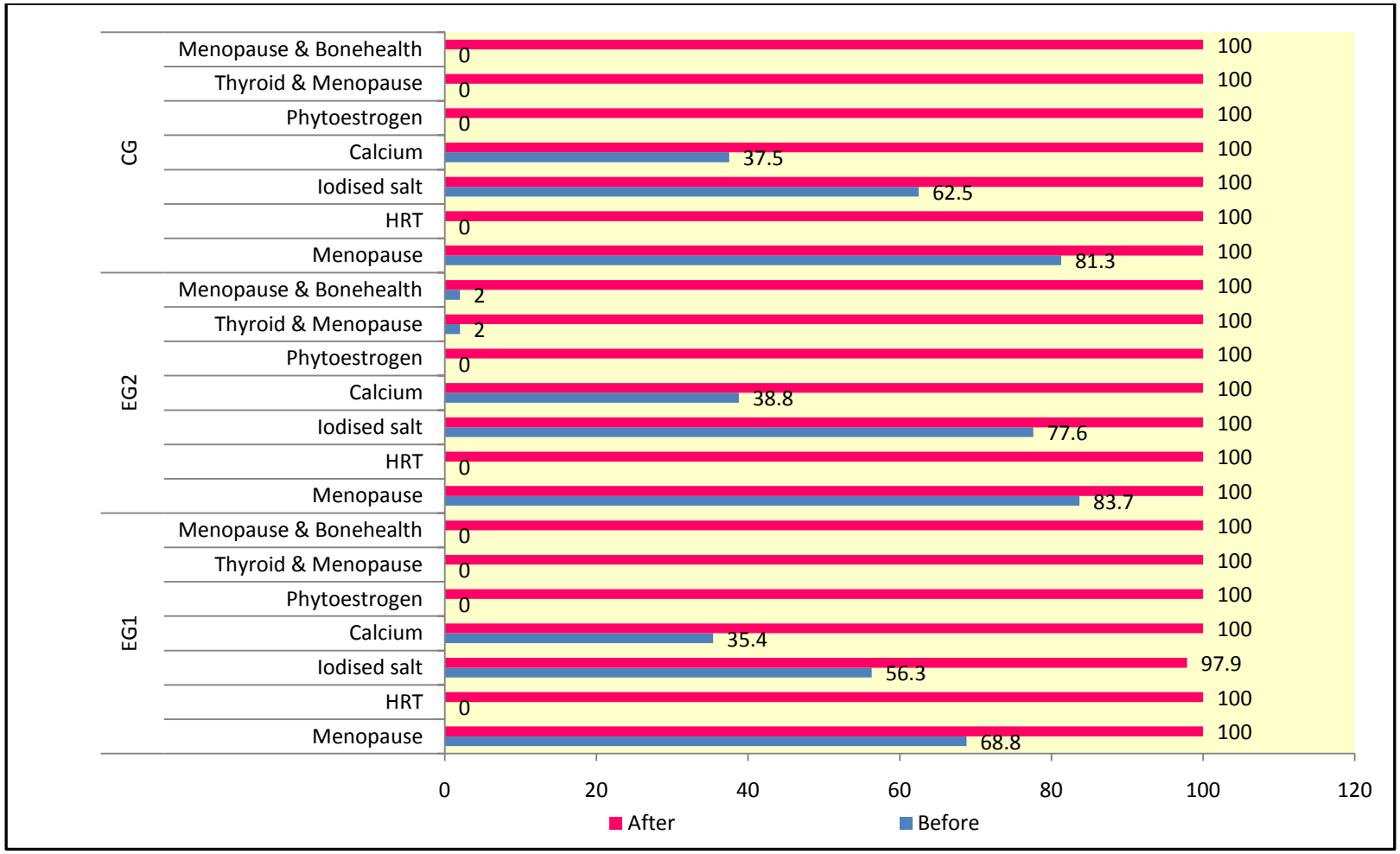


Figure 4.29: Effect of intervention on knowledge level - amongst experimental (EG1 and EG2) and control (CG) groups

Table 4.27: Level of significance for improvement in knowledge (p-value)

Particulars	EG1	EG2	CG
Awareness about menopause	<0.001***	0.005	0.003
Awareness about HRT	<0.001***	<0.001***	<0.001***
Awareness about Iodised salt	<0.001***	0.001	<0.001***
Awareness about Calcium	<0.001***	<0.001***	<0.001***
Awareness about Phytoestrogen	<0.001***	<0.001***	<0.001***
Relation of thyroid and menopause	<0.001***	<0.001***	<0.001***
Relation of menopause and bone	<0.001***	<0.001***	<0.001***

Significantly different at p<0.05, p<0.01**, p<0.001**

Table4.28: Awareness about onset age for menopause – before and after intervention

Group	Before intervention- n, (%)				After Intervention- n, (%)				p-value
	33-45 Yrs	45-55 Yrs	>55 Yrs	No idea	33-45 yrs	45-55 yrs	>55 yrs	No idea	
EG1	19 (39.6)	11 (22.9)	1 (2.1)	17 (35.4)	1 (2.1)	47 (97.9)	0 (0)	0 (0)	0.018*
EG2	13 (26.5)	18 (36.7)	5 (10.2)	13 (26.5)	0 (0)	49 (100)	0 (0)	0 (0)	0.012*
CG	13 (27.1)	21 (43.8)	0 (0)	14 (29.2)	0 (0)	48 (100)	0 (0)	0 (0)	0.003**

Significantly different at p<0.05, p<0.01*

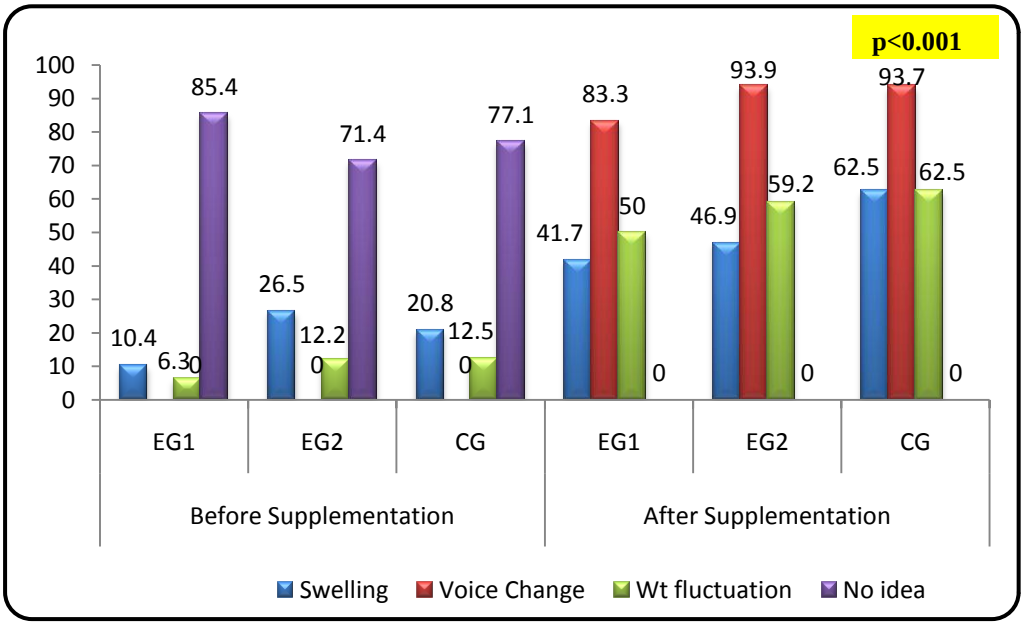


Figure 4.30: Percent responses for symptoms of thyroid – before and after intervention

Table4.29: Percent responses for importance of iodised salt – before and after intervention

	Before Intervention N,(%)			After Intervention N, (%)		
	EG1	**EG2**	**CG**	**EG1**	**EG2**	**CG**
Good Health	4 (8.3)	0 (0)	1 (2.1)	11 (22.9)	8 (16.3)	10 (20.8)
Mental change Development	1 (2.1)	3 (6.1)	1 (2.1)	42 (87.5)	36 (73.4)	37 (77.1)
To avoid thyroid	1 (2.1)	4 (8.2)	3 (6.3)	37 (77.1)	48 (97.9)	46 (93.9)
No idea	42 (87.5)	42 (85.7)	43 (89.6)	0 (0)	0 (0)	0 (0)
p-significance				***	***	***

Significantly different at p<0.001***

Table 4.30: Percent responses for importance of calcium – before and after intervention

	Before Intervention N, (%)			After Intervention N,(%)		
	EG1	**EG2**	**CG**	**EG1**	**EG2**	**CG**
For bone health	12 (25)	11 (22.4)	11 (22.9)	48 (100)	49 (100)	48 (100)
No idea	36 (75)	38 (77.6)	37 (77.1)	0 (0)	0 (0)	0 (0)
p-significance				***	***	***

Significantly different at p<0.001***

Table 4.31: Percent responses for sources of calcium – before and after intervention

	Before Intervention N, (%)			After Intervention N, (%)		
	EG1	**EG2**	**CG**	**EG1**	**EG2**	**CG**
Milk and its products	7 (14.6)	14 (28.6)	9 (18.7)	41 (85.4)	21 (42.8)	43 (89.6)
Banana/Fruit	11 (22.9)	17 (34.7)	11 (22.9)	37 (77.1)	33 (67.3)	23 (47.9)
Eggs and Poultry	0 (0)	4 (8.2)	1 (2.1)	21 (43.7)	45 (91.8)	34 (70.8)
GLFs	4 (8.3)	4 (8.2)	4 (8.3)	0 (0)	0 (0)	0 (0)
No idea	34 (70.8)	31 (63.3)	36 (75)	0 (0)	0 (0)	0 (0)
p-significance				***	***	***

Significantly different at p<0.001***

For the thyroid related symptoms, majority replied they did not know at baseline. The percent response was improved for weight fluctuation, change in voice followed by swelling in all study groups after an intervention ($p<0.001$).

Iodized salt is good for mental development and for thyroid functioning, was reported only by 4.2% women in EG1, 14.3% in EG2 and 8.4% women in CG. These percent responses were significantly increased to 80% to 90% ($p<0.001$).

The responses about importance of calcium and its sources were also very poor in study population at baseline, and showed significant increased after an intervention ($p<0.001$).

Similar results were reported by study conducted in Karachi (2008) on postmenopausal women. Out of one hundred and two postmenopausal women, 97% women heard about menopause, 29.4% were aware with

menopausal symptoms and only 1.96% respondents were aware of HRT. The author also stated that lack of knowledge was high in less educated, older and poor socio-economic class. (Malik HS, 2008) The findings of studies conducted by Maharaj et al., (2007), Mazhar et al., (2003) and Kaufert et al., (1998) are comparable to this.

In the present study, the reason for having less knowledge on menopause, its symptoms, HRT etc might be the women were never reported such transitional issues and consulted the doctors and who consulted to doctors, those were not advised by doctors to use HRT.

Studies performed in Iran in the field of investigating the level of women's knowledge and attitude toward menopause indicate inadequate knowledge and negative attitude toward this phenomenon among Iranian women. (Noroozi et al., 2013; Hasan Pour Azghadi B, Abbasi Z, 2006; Hassanzadeh et al., 2003; EftekhariTavakoli et al., 1999)

In contrary to above findings, Kaur, Walia and Singh (2005) reported that the 84% of women in north India had prior knowledge about menopause and the most surprising fact in the study was about 47% of the women reported that they were prepared in advance for menopause, 67% of women had discussed menopause with their friends, 78% had discussed it with their husbands. Such knowledge and awareness were lacking in our population.

Education and intervention programs on menopause symptoms are thought to be essential in middle-aged women.

4.3.6 Consumption frequency of Phytoestrogen, Iron and Iodine rich foods

The consumption pattern of phytoestrogen rich foods revealed, daily consumption of phytoestrogenic food was very poor in all study groups. Foods like onion, cabbage were consumed more frequently followed by mung beans, fenugreek seeds, sesame seeds; and dates and almonds were consumed at a lower frequency.

After an intervention, marked improvement was reported for daily consumption of phytoestrogen rich foods.

Apart from supplementation provided to experimental groups, fenugreek seeds, sesame seeds, dates were incorporated to their daily diet by all study groups. The consumption frequency of onion and mung beans were more acceptable by the women.

In the present study, consumption frequency of iron rich foods revealed (at baseline) wheat flour was the most consumed (EG1-25% , EG2-29% , CG- 22%, on daily basis) food followed by puffed rice, rice flakes, bajra and bengalgram moderately consumed foods. While the food items like soybean, jowar, raisins, almonds were not consumed at significant frequency. The similar pattern was observed amongst all study groups.

After an intervention, percent responses were improved for consumption of fenugreek, seasame seeds, wheat flour and puffed rice. While consumption of food items like almonds, raisins, dates were not improved much, this could be due to the lower socio-economic profile of the population.

The food items like jowar and soybean were not much acceptable by the study population.

For consumption of iodine rich foods amongst all study groups, milk and milk products were the chief source and consumed daily by half of the population. Most of the women were vegetarian; 83.3% in EG1, 61.2% in EG2 and 85.4% in CG. Though few were consuming eggs moderately ; 66.7% in EG1, 44.9% in EG2 and 70.8% in CG.

There was a marked increase in consumption frequency of spinach in control group in comparison to experimental groups. There was no much diffrence observed for consumption of other foods items.

Food frequency analysis showed, consumption pattern of phytoestrogen, ioidne and iron rich food were parallelamong experimental and control groups. The improvement noted after an intervention, also found similar in all study groups.

This also suggests, if the women may aware and sensitize for available phytoestrogen, iodine and iron rich sources, they are willing to incorporate these into their routine diet.

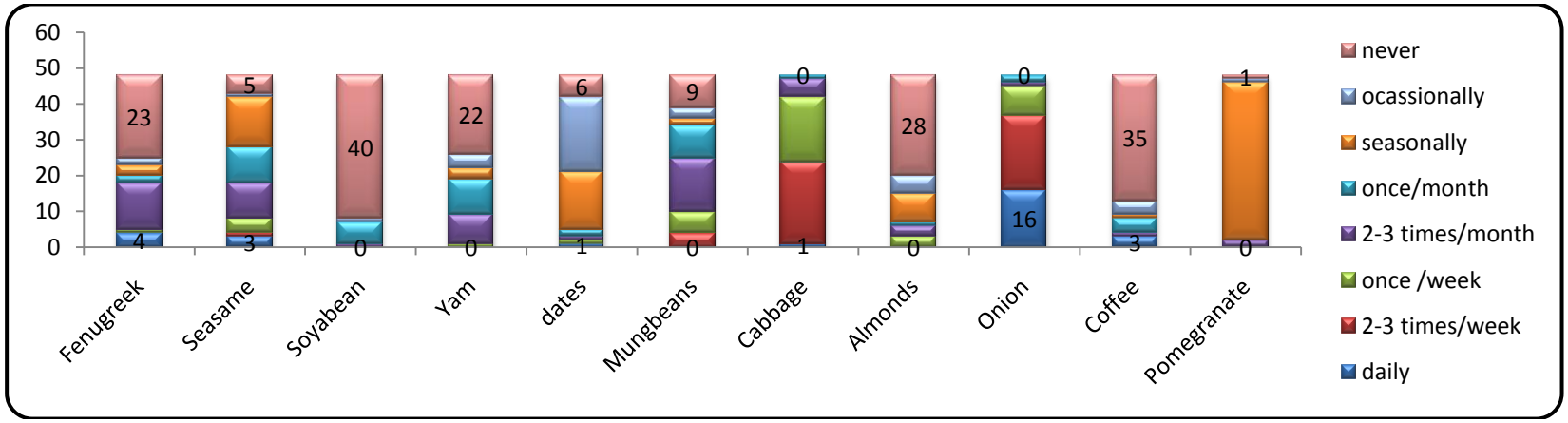


Figure 4.31:Consumption pattern of major phytoestrogen rich foods in EG1 (Before intervention)

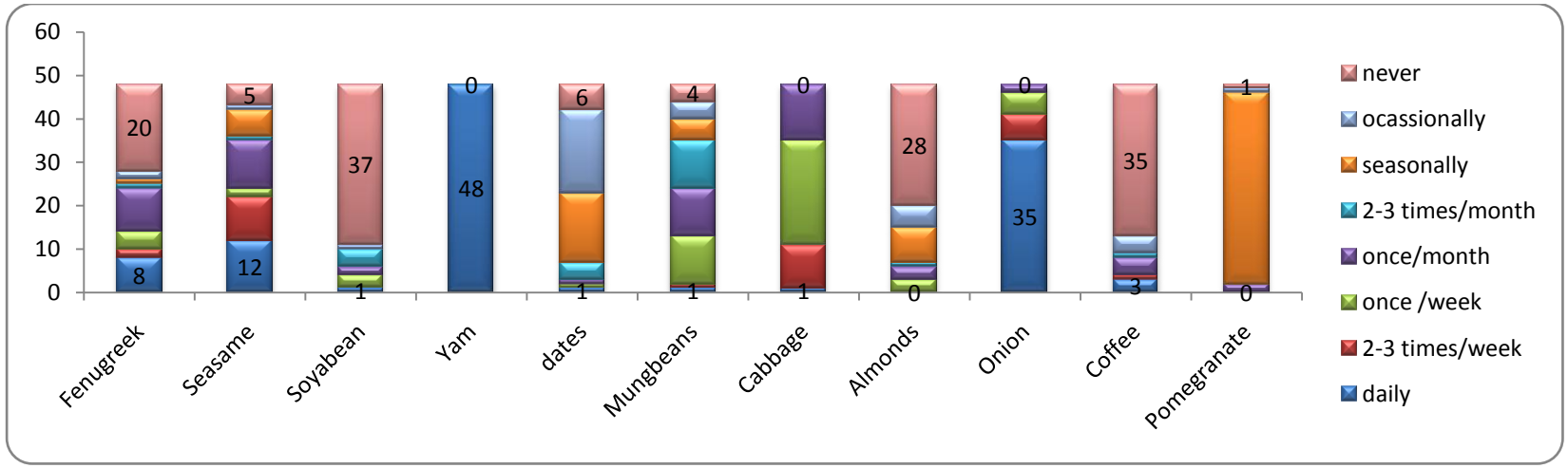


Figure 4.32: Consumption pattern of major phytoestrogen rich foods in EG1 (After intervention)

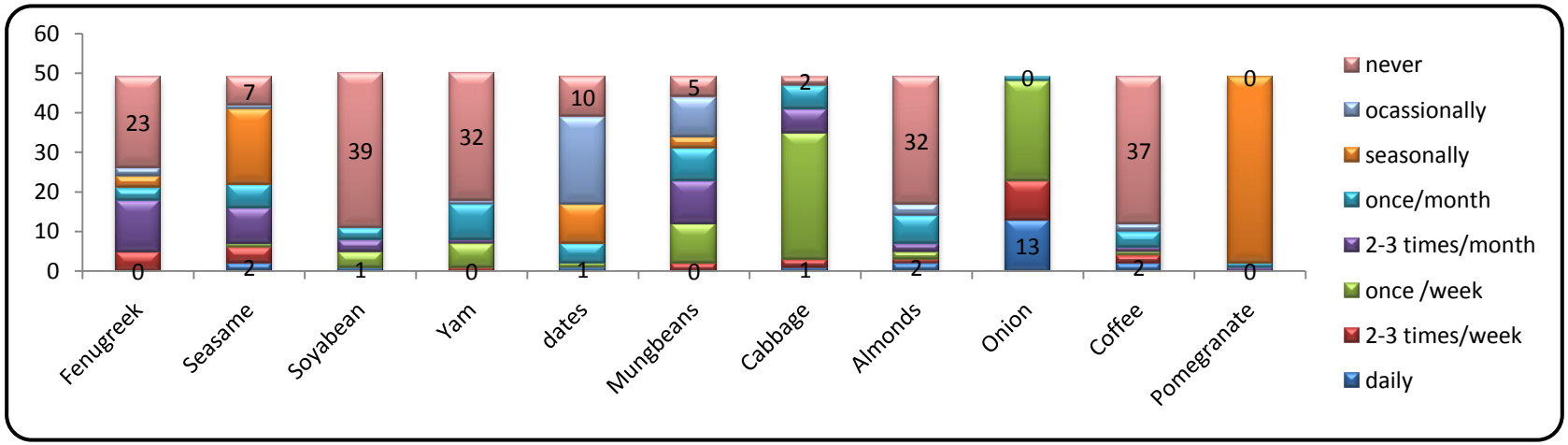


Figure 4.33: Consumption pattern of major phytoestrogen rich foods in EG2 (Before Intervention)

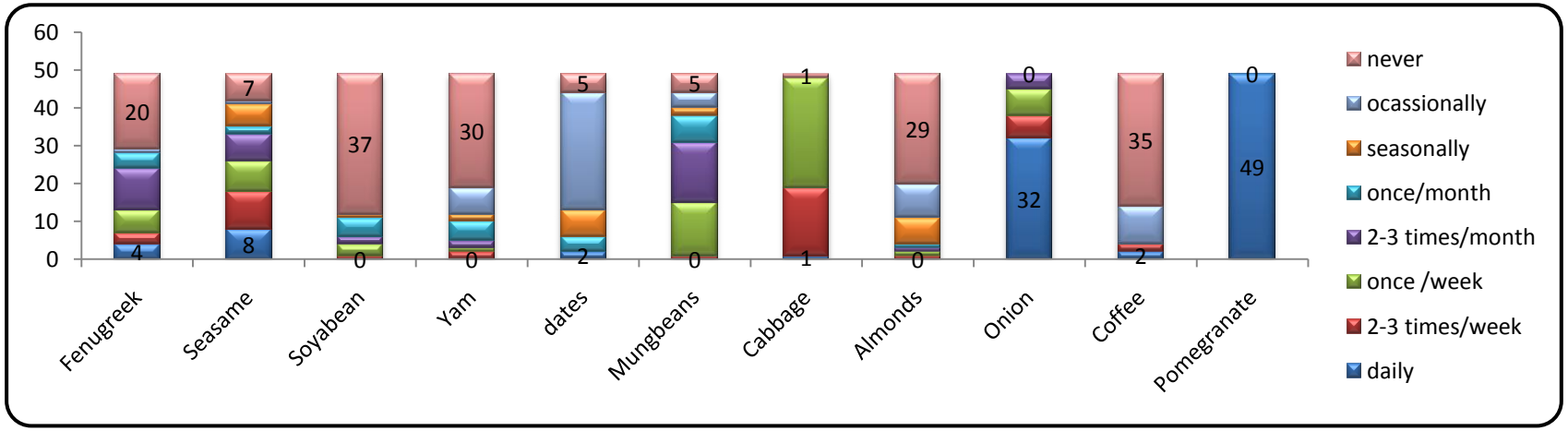


Figure 4.34: Consumption pattern of major phytoestrogen rich foods in EG2 (After Intervention)

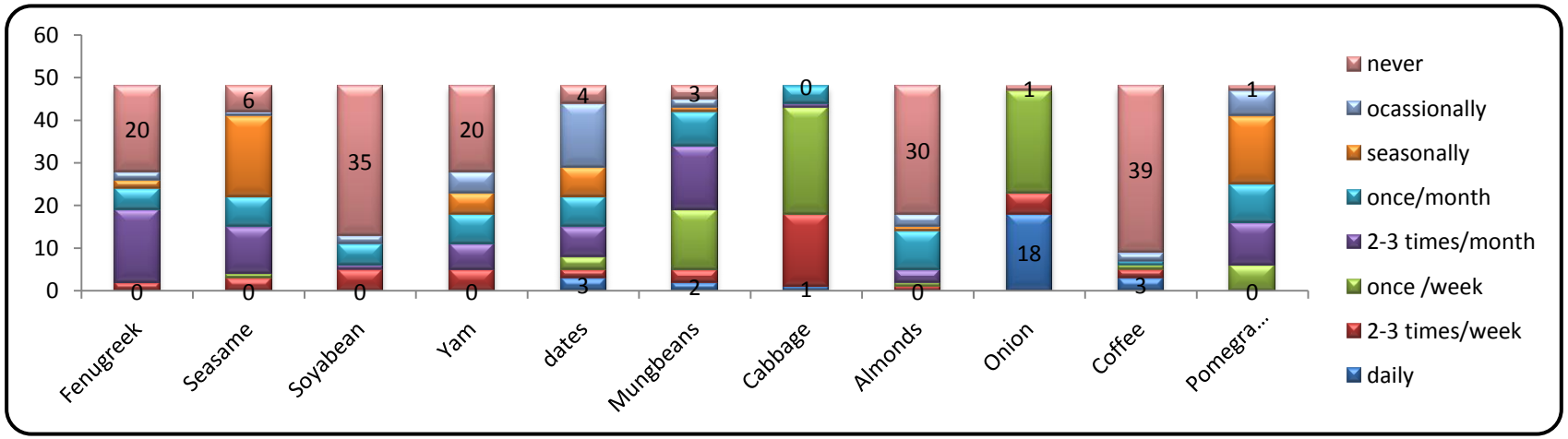


Figure 4.35:Consumption pattern of phytoestrogen rich foods in CG (Before Intervention)

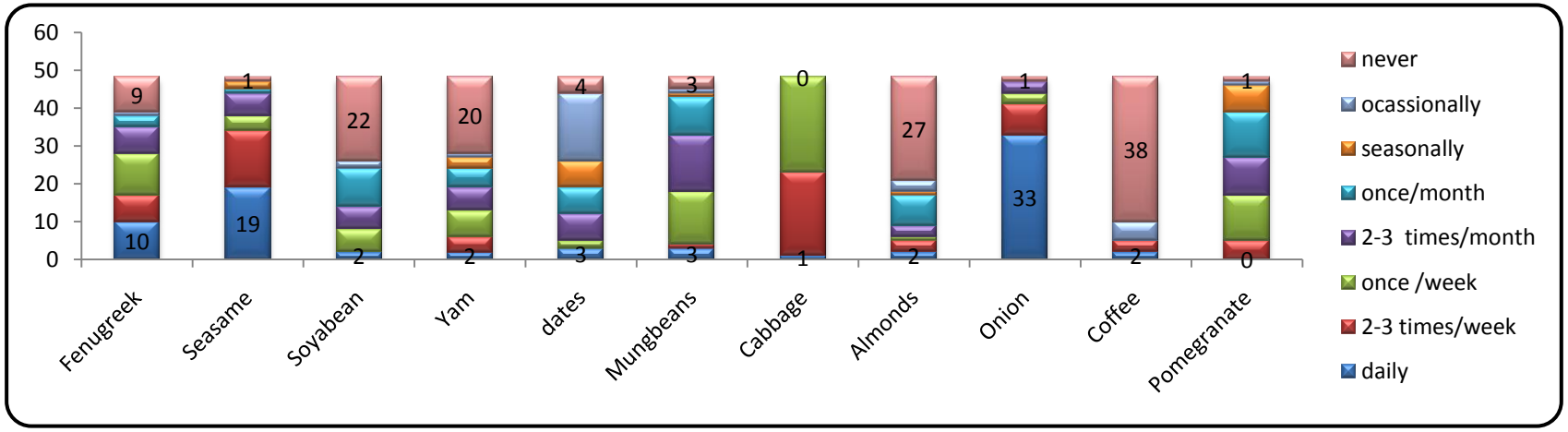


Figure 4.36: Consumption pattern of phytoestrogen rich foods in CG (After Intervention)

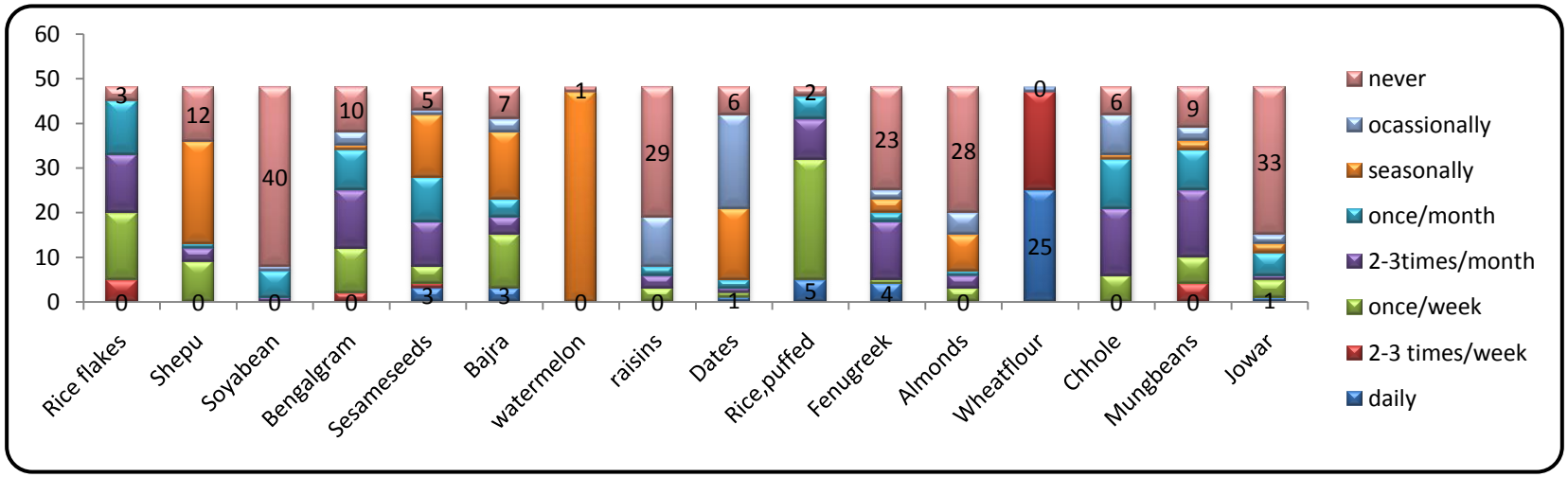


Figure 4.37:Consumption frequency of selected Iron rich foods in EG1 (Before intervention)

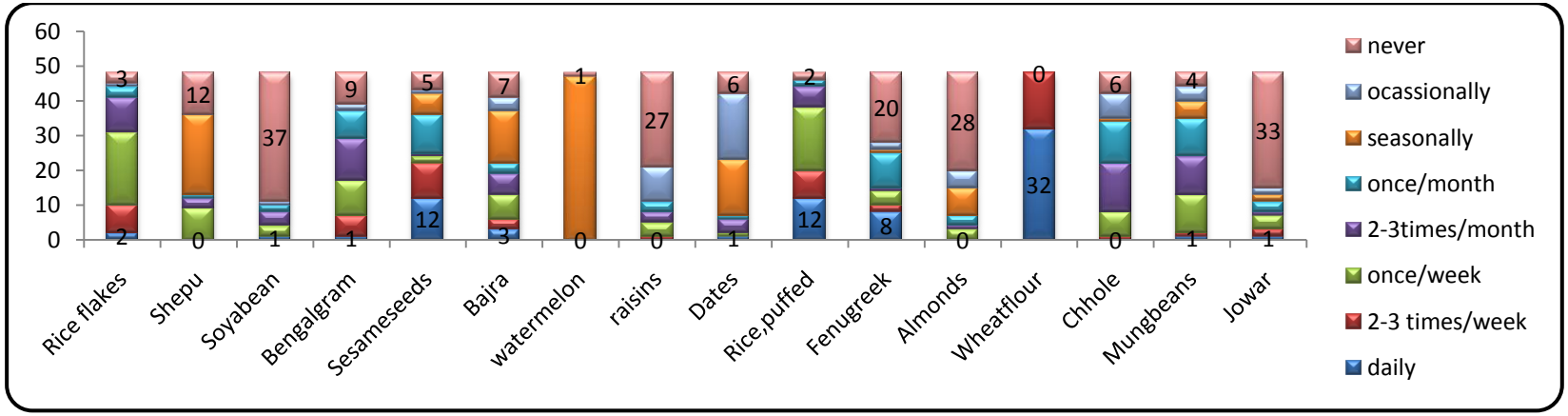


Figure 4.38 : Consumption frequency of selected Iron rich foods in EG1 (After intervention)

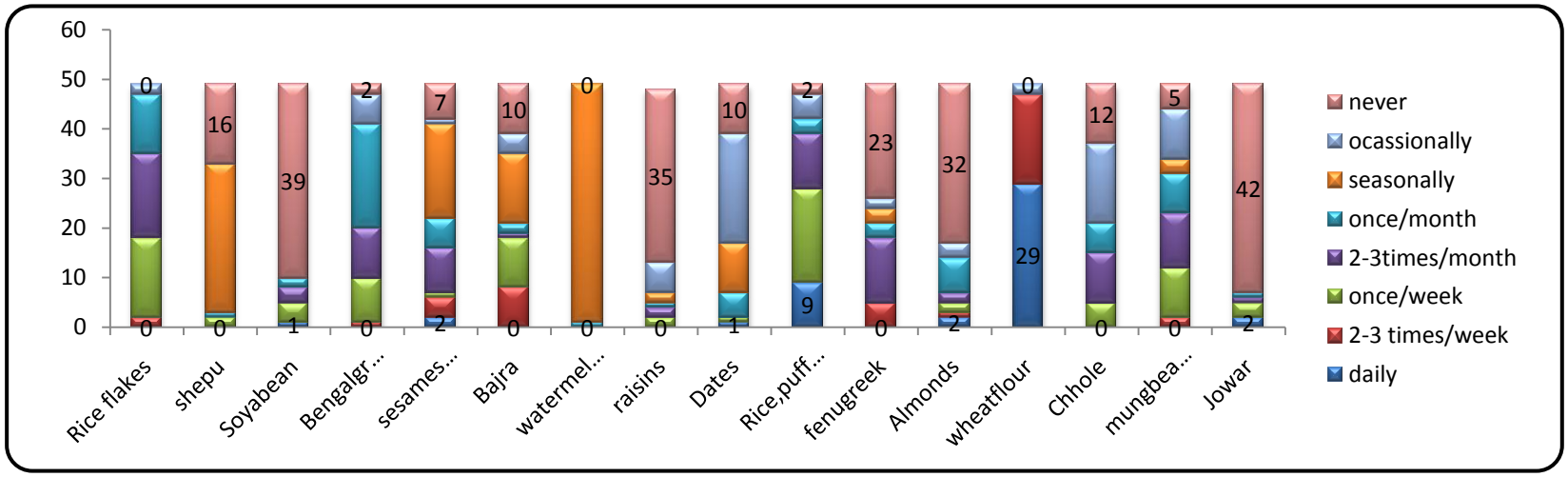


Figure 4.39: Consumption frequency of selected Iron rich foods in EG2 (Before intervention)

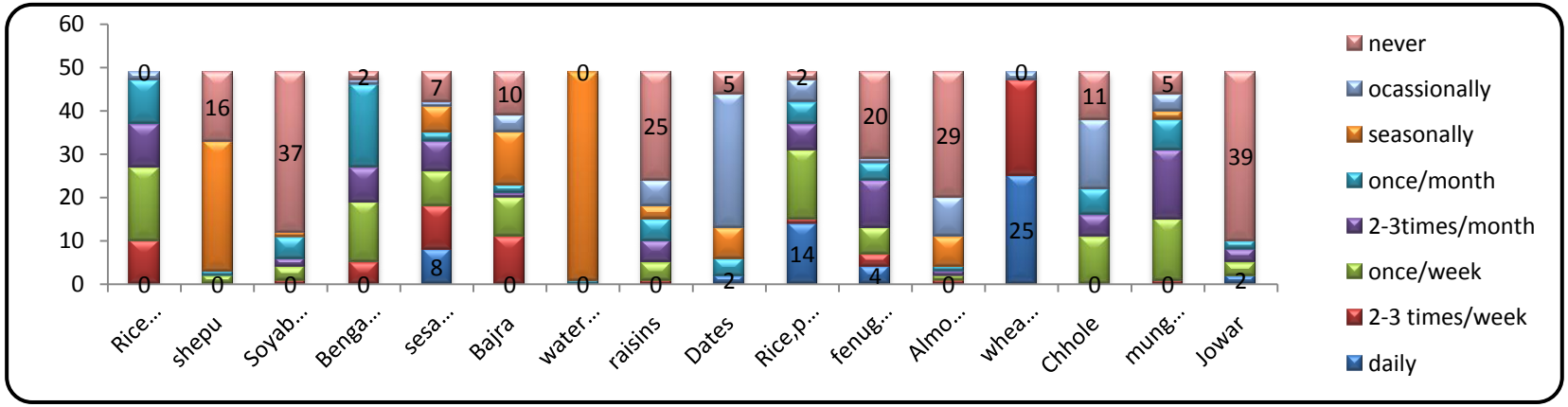


Figure 4.40: Consumption frequency of selected Iron rich foods in EG2 (After intervention)

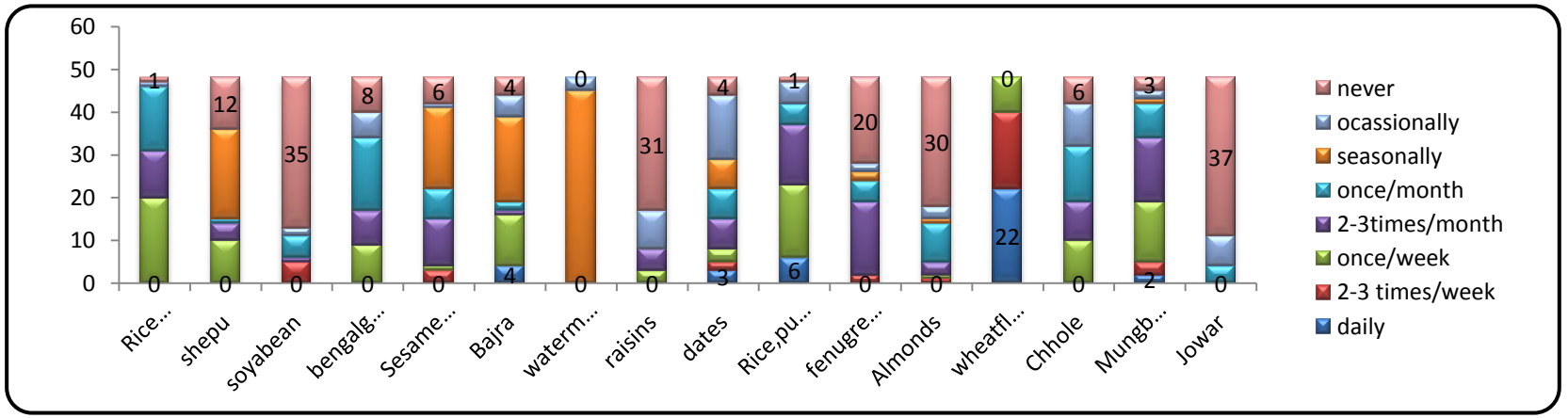


Figure 4.41: Consumption frequency of selected Iron rich foods in CG (Before intervention)

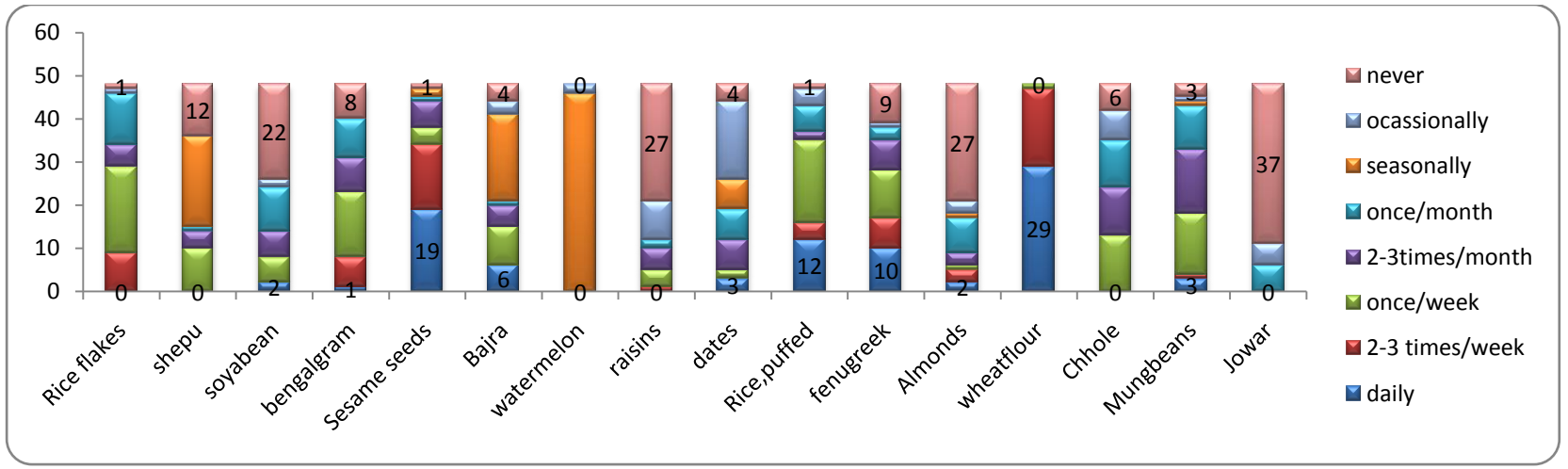


Figure 4.42: Consumption frequency of selected Iron rich foods in CG (After intervention)

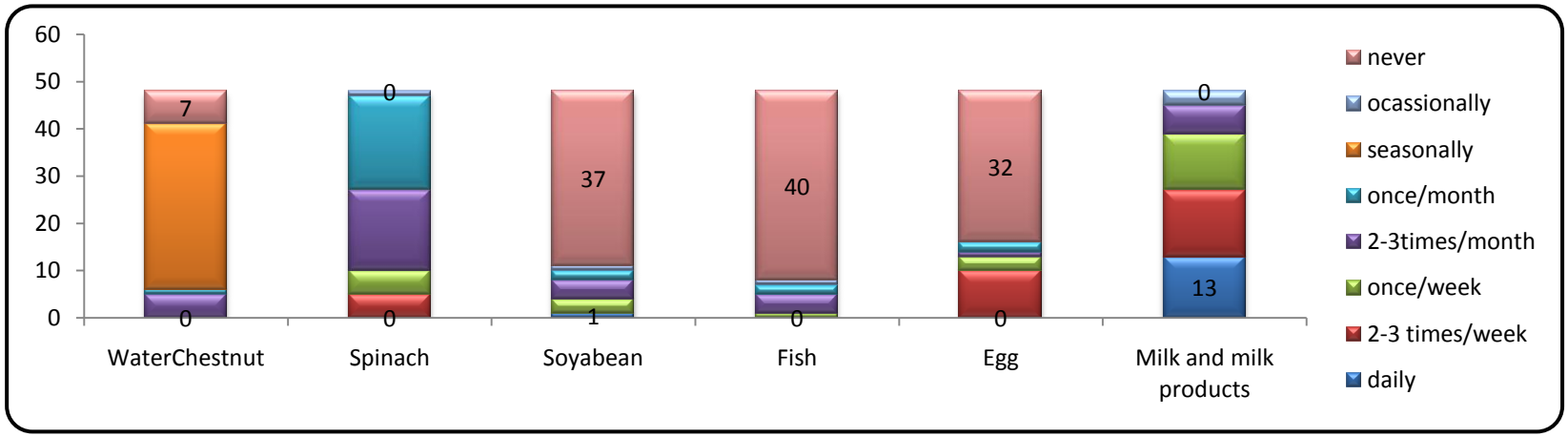


Figure 4.43: Consumption pattern of major Iodine rich foods in EG1 (Before intervention)

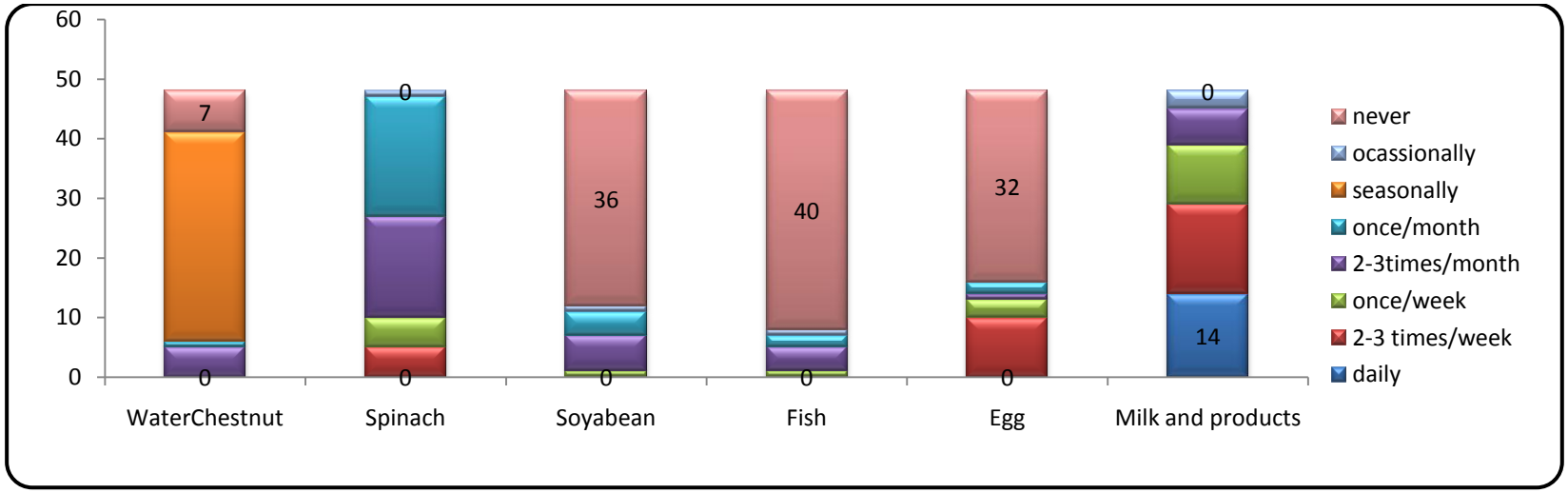


Figure 4.44: Consumption pattern of major Iodine rich foods in EG1 (After intervention)

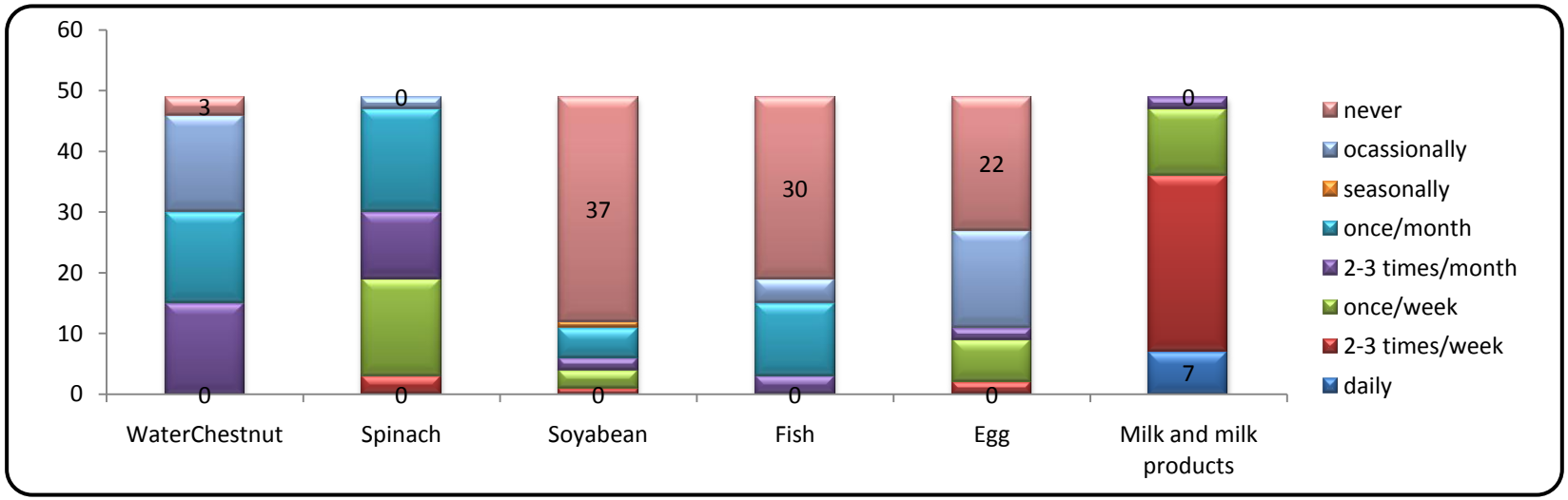


Figure 4.45: Consumption pattern of major Iodine rich foods in EG2 (Before intervention)

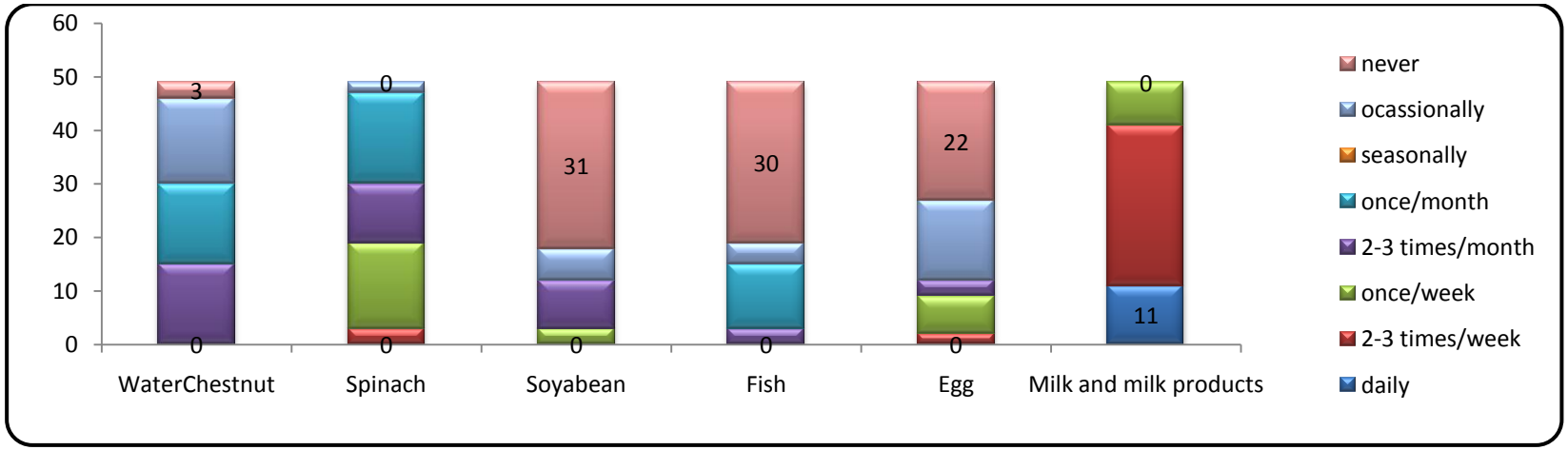


Figure 4.46: Consumption pattern of major Iodine rich foods in EG2 (After intervention)

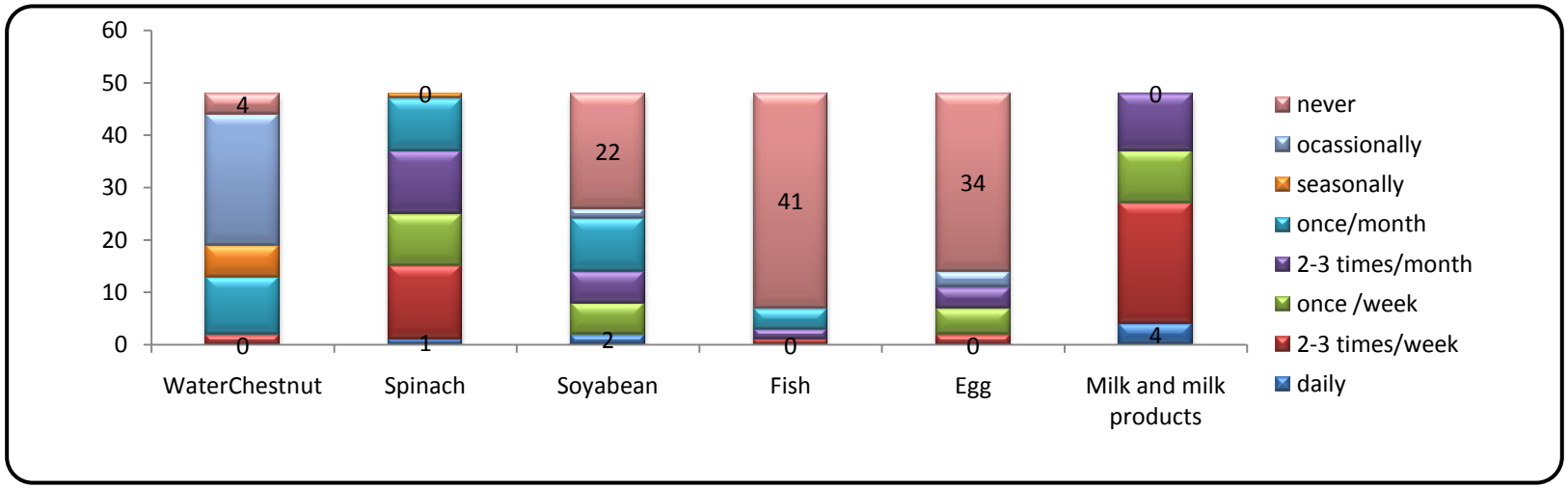


Figure 4.47: Consumption pattern of major Iodine rich foods in CG (Before intervention)

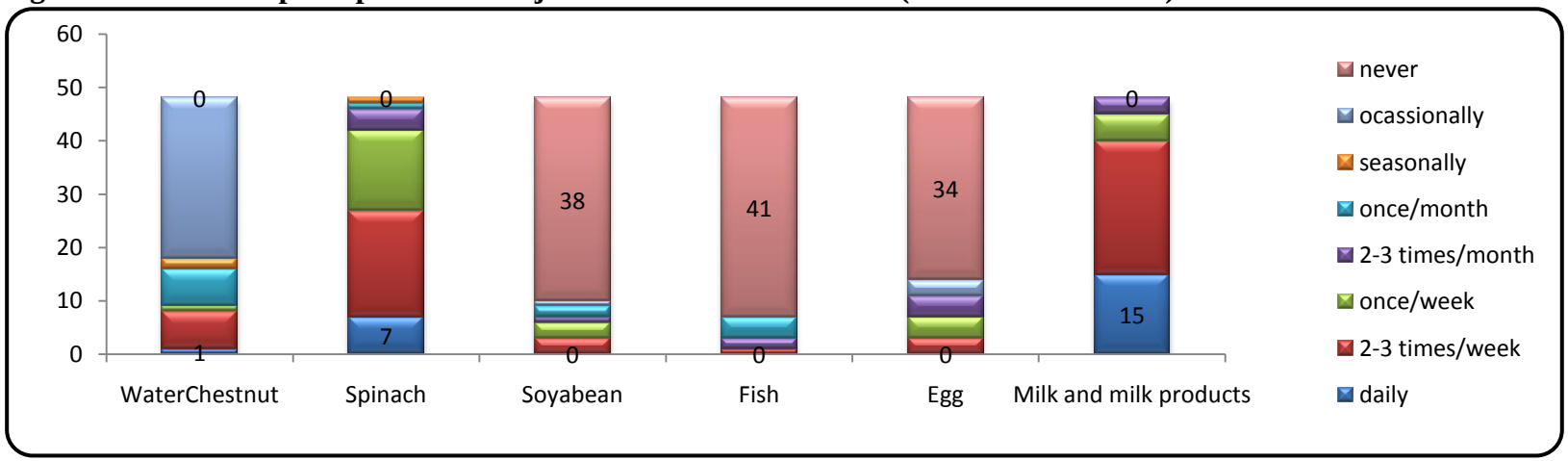


Figure 4.48: Consumption pattern of major Iodine rich foods in CG (After intervention)

Phytoestrogens elicit gene expression changes in reproductive tissues, confirming that they are biologically active in a living system. The doses at which these effects occur are quite variable, are tissue dependent, and are most likely due to the interaction of either ERα or ERβ within a given tissue. For example, the ovary expresses the highest level of ERβ in the body and genistein and daidzein preferentially bind to ERβ, so one might anticipate that phytoestrogens in general may have greater effects on the ovary itself. Further research studies need to be conducted to demonstrate this possibility.In comparison to synthetic estradiol, effects of phytoestrogen may be smaller; there are no adverse side effects like propagation of hormone-sensitive tumours associated with phytoestrogen consumption. (Schilling et al., 2013)

Zhao and Mu (2011) also speculated that phytoestrogen might not exhibit any significant toxicity or side-effects on the healthy reproductive organs.

Due to the structural similarities with 17-β estradiol, isoflavones are able to bind to estrogen receptors (ERs). Activation of ERs initiates a cascade of intracellular mechanisms, which may include control of the activity of G-proteins, adenylatecyclase, phospholipase or protein kinase. (Simoncini et al., 2003)

The activation cascades affects cell metabolism, changes in cell permeability, ion concentration, production of NO etc. This mechanism is associated with rapid vasodilation of blood vessels due to increased activity of endothelial NO-synthase. (Pechanova and Simko, 2007; Vera et al., 2007; Liu et al., 2004)

In the CNS, the non-genomic way of action may affect excitability of neurons due to changes in cell membrane permeability (McEwen &Alves, 199) These processes may be related to the effects of estradiol and isoflavone phytoestrogens on cognitive functions.

Phytoestrogens are promising therapeutic alternative not only to get relief in menopausal transition but also for the suppression of fat accumulation. This was we observed in our study population also, where experimental groups reported the significant decrease in waist circumference as well weight reduction. The other lifestyle approaches like laughing and stretching exercise, yoga helped in mobilization of fat but not strong enough for weight reduction during stipulated study duration.

The studies reported that, the high isoflavone levels increase the activity of both 5α-reductase, which catalyzes the conversation of testosterone to 5α-dihydrosterone, and aromatase P450 which mediates the conversion of testosterone to estradiol. (Almstrup et al., 2002; Kao et al., 1998; Evans et al., 1995; Aldercreutz et al., 1993)

The same physiological effect of phytoestrogen might be contributed to improvement of estradiol in our study population after supplementation of pomegranate and elephant foot yam. While in the control group (did not receive phytoestrogen supplementation not) improvement in serum estradiol was not noticed.

Coumestrol have shown the inhibitory effect on GnRH gene expression in the GnRH neuron, which elicited an inhibitory regulation on the reproductive system via binding to ERβ. The studies have reported the GnRH-inhibited effect of coumestrol and selective endocrine activity of genistein led to reducing LH release at the level of rat pituitary (Mcgarvey et al., 2001; Hughes et al., 1991)

The present study confirms and demonstrates that food-derived phytoestrogen modulate the balance between gonadotropin hormones and estradiol level, which results into the overall relief in menopausal symptoms among perimenopausal women.

4.4 PHASE 4

This phase mainly designed to contribute and compensate the women of control group, as they were provided with phytoestrogen supplementation.

As the supplementation proved beneficial in terms of relief in menopausal symptoms and hormone levels, a booklet "Menopause-and Its Management" was developed in local language (Gujarati). The points like basic information on menopause and its transitions, the frequency and severity of menopause symptoms, long-term effects of estrogen loss and side effects of HRT, use of available therapies and role of laughing and stretching exercise, yoga to enhance health were included along with findings of supplementation phase (Phase III). This booklet was distributed to women enrolled in control group.

The details covered in the booklet were shown in Figure 4.60.

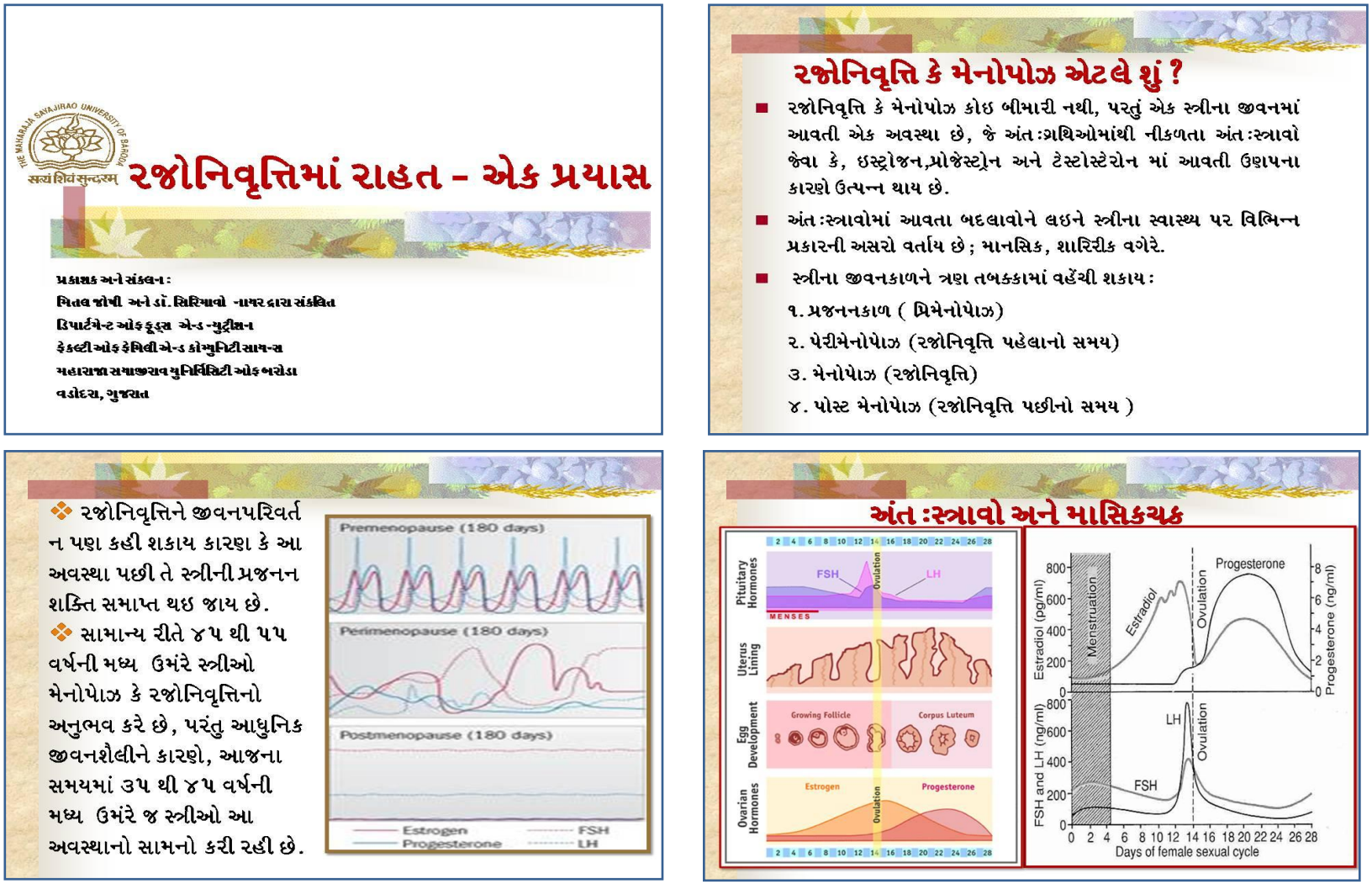
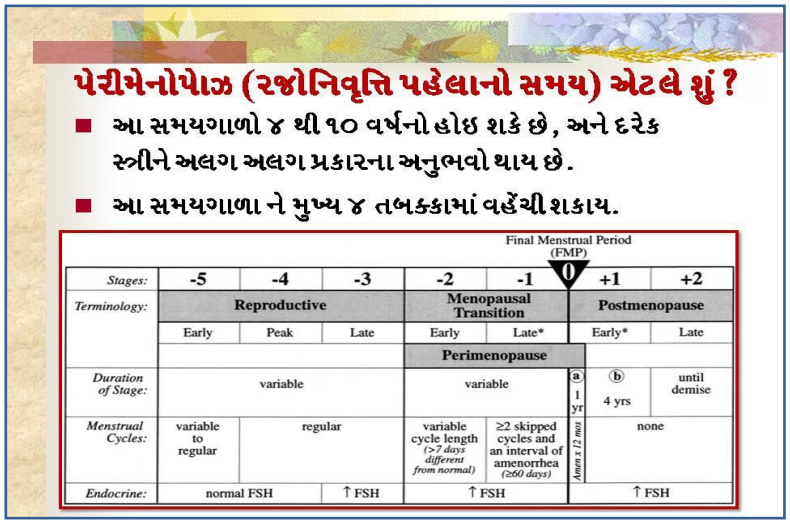
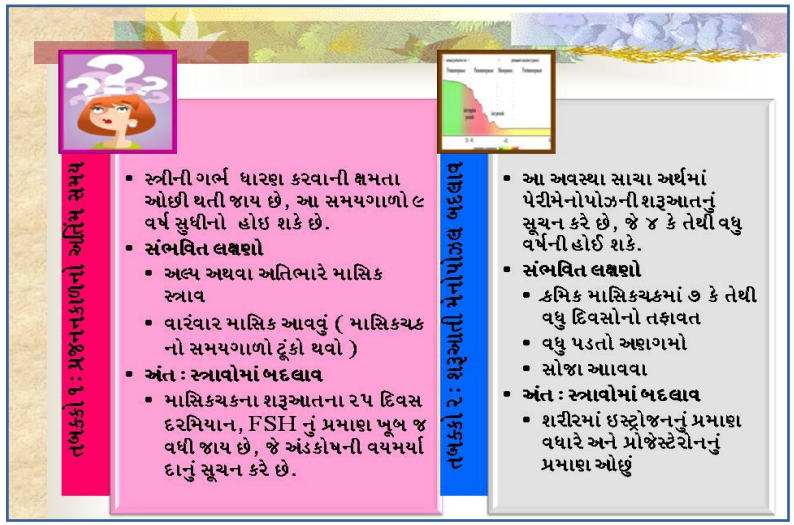
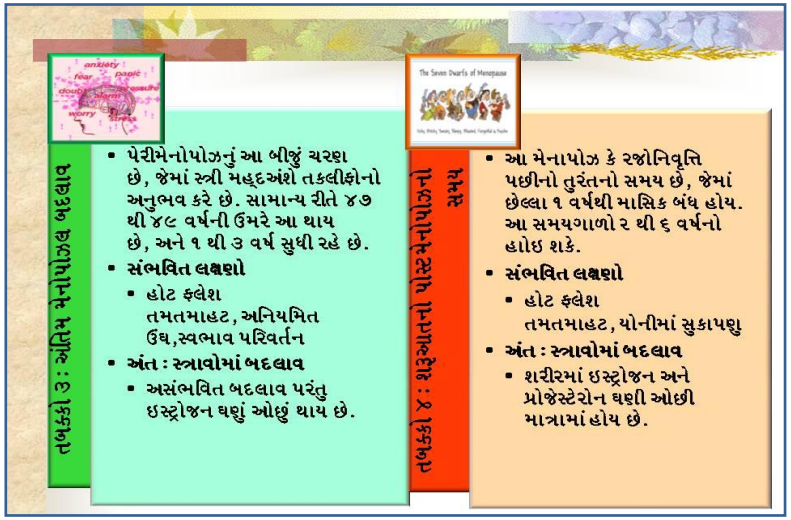


Figure 4.49: Overview of a booklet - "Menopause-and Its Management"

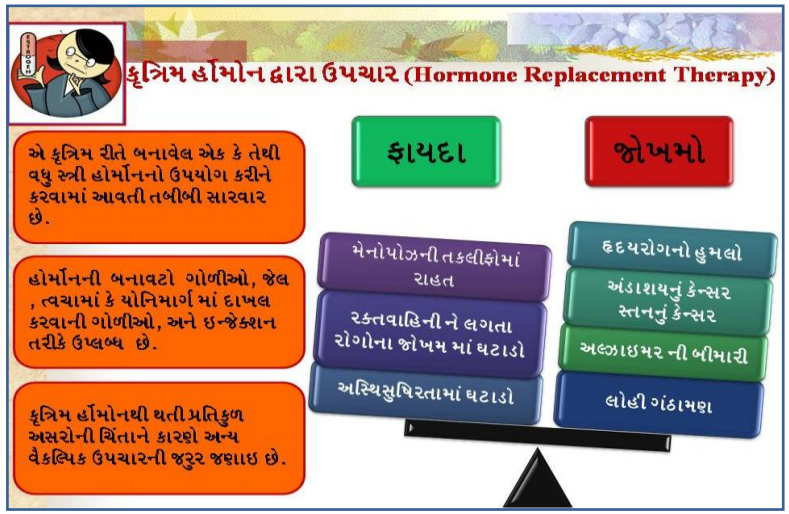

પેરીમેનોપોઝ (રજોનિવૃત્તિ પહેલાનો સમય) એટલે શું ?
આ સમયગાળો ૪ થી ૧૦ વર્ષનો હોઇ શકે છે, અને દરેક સ્ત્રીને અલગ અલગ પ્રકારના અનુભવો થાય છે.
આ સમયગાળા ને મુખ્ય ૪ તબક્કામાં વહેંચી શકાય.
Final Menstrual Period (FMP)
Stages: -5 -4 -3 -2 -1 0 +1 +2
Terminology: Reproductive Menopausal Transition Postmenopause
Early Peak Late Early Late* Early* Late
Perimenopause
Duration of Stage: variable variable a 1 yr b 4 yrs until demise
Menstrual Cycles: variable to regular regular variable cycle length (>7 days different from normal) ≥2 skipped cycles and an interval of amenorrhea (≥60 days) Amen x 12 mos none
Endocrine: normal FSH ↑ FSH ↑ FSH ↑ FSH


તબક્કો ૧ : પ્રજનનકાળનો અંતિમ સમય
સ્ત્રીની ગર્ભ ધારણ કરવાની ક્ષમતા ઓછી થતી જાય છે, આ સમયગાળો ૯ વર્ષ સુધીનો હોઇ શકે છે.
સંભવિત લક્ષણો
અલ્પ અથવા અતિભારે માસિક સ્ત્રાવ
વારંવાર માસિક આવવું (માસિકચક્ર નો સમયગાળો ટૂંકો થવો)
અંત : સ્ત્રાવોમાં બદલાવ
માસિકચક્રના શરૂઆતના ૨૫ દિવસ દરમિયાન, FSH નું પ્રમાણ ખૂબ જ વધી જાય છે, જે અંડકોષની વયમર્યાદાનું સૂચન કરે છે.
તબક્કો ૨ : શરૂઆતી મેનોપોઝ બદલાવ
આ અવસ્થા સાચા અર્થમાં પેરીમેનોપોઝની શરૂઆતનું સૂચન કરે છે, જે ૪ કે તેથી વધુ વર્ષની હોઈ શકે.
સંભવિત લક્ષણો
ક્રમિક માસિકચક્રમાં ૭ કે તેથી વધુ દિવસોનો તફાવત
વધુ પડતો અણગમો
સોજા આવવા
અંત : સ્ત્રાવોમાં બદલાવ
શરીરમાં ઇસ્ટ્રોજનનું પ્રમાણ વધારે અને પ્રોજેસ્ટેરોનનું પ્રમાણ ઓછું

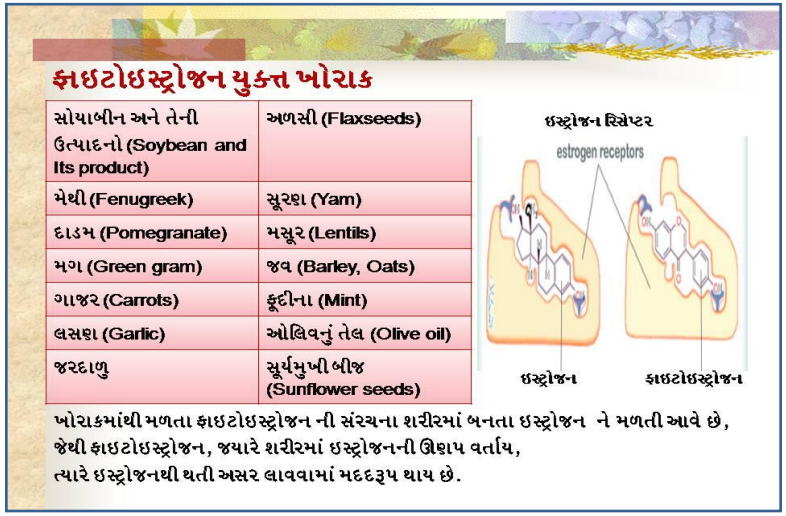

તબક્કો ૩ : અંતિમ મેનોપોઝ બદલાવ
પેરીમેનોપોઝનું આ બીજું ચરણ છે, જેમાં સ્ત્રી મહદ્અંશે તકલીફોનો અનુભવ કરે છે. સામાન્ય રીતે ૪૭ થી ૪૯ વર્ષની ઉંમરે આ થાય છે, અને ૧ થી ૩ વર્ષ સુધી રહે છે.
સંભવિત લક્ષણો
હોટ ફ્લેશ તમતમાહટ, અનિયમિત ઉંઘ,સ્વભાવ પરિવર્તન
અંત : સ્ત્રાવોમાં બદલાવ
અસંભવિત બદલાવ પરંતુ ઇસ્ટ્રોજન ઘણું ઓછું થાય છે.
તબક્કો ૪ : શરૂઆતનો પોસ્ટમેનોપોઝનો સમય
આ મેનાપોઝ કે રજોનિવૃત્તિ પછીનો તુરંતનો સમય છે, જેમાં છેલ્લા ૧ વર્ષથી માસિક બંધ હોય. આ સમયગાળો ૨ થી ૬ વર્ષનો હોઇ શકે.
સંભવિત લક્ષણો
હોટ ફ્લેશ તમતમાહટ, યોનીમાં સુકાપણુ
અંત : સ્ત્રાવોમાં બદલાવ
શરીરમાં ઇસ્ટ્રોજન અને પ્રોજેસ્ટેરોન ઘણી ઓછી માત્રામાં હોય છે.

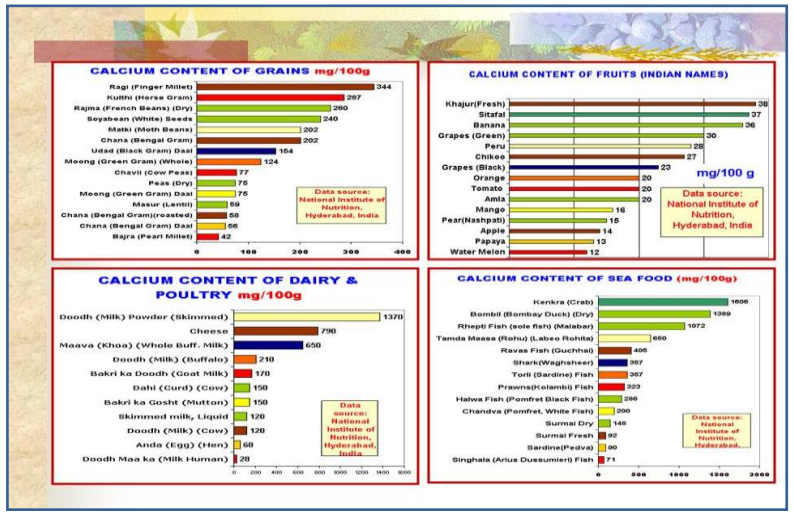

પેરીમેનોપોઝ અને મેનોપોઝ ના લક્ષણો
VASOMOTOR SYMPTOMS (તકલીફો)
Hot Flashes
Palpitation
Headache
Night Sweat
તમતમાહટ, ધબકારા, માથાનો દુખાવો, રાત્રિસ્વેદ
GENITAL PROBLEMS યોનીમાર્ગની તકલીફો
VAGINAL યોનીમાં
DRYNESS સુકાપણું
BURNING બળતરા
ITCHING ખૂજલી
IRRITION, ચીરા, ચાંદી
DISCHARGE સફેદ પાણી
DYSPARUNIA સંભોગ સમયે દુઃખાવો
SEX - DISLIKE સંભોગની અનિચ્છા
URINARY PROBLEMS પેશાબમાં થતી તકલીફો
FREQUENCY વારંવાર જવું
BURNING બળતરા થવી
DYSUREA દુઃખાવો
RETENTION ભરાવો
INCONTINENCE URGE STRESS
PSYCHOLOGICAL માનસીક તકલીફો
TIREDNESS થાક
TENSION તણાવ
ANGER ગુસ્સો
DEPRESSION હતાશા
FOGETFULNESS યાદદાસ્ત ઓછી થવી
SWINGING MOOD મુડ બદલાવ
INSOMNIA ઉંઘ ન આવવી
SUICIDE આપઘાત

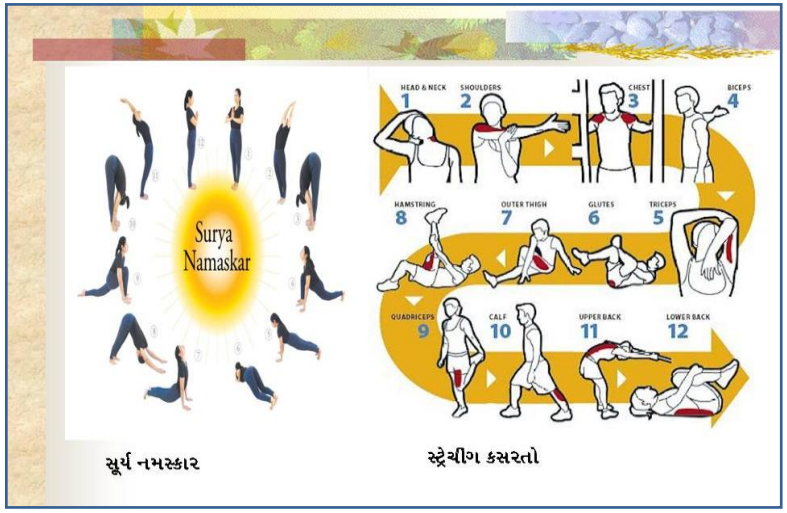

પેરીમેનોપોઝ અને મેનોપોઝની તકલીફોમાં રાહત માટે સારવાર
કૃત્રિમ હોર્મોન દ્વારા ઉપચાર
(Hormone Replacement Therapy)
જડીબુટ્ટીઓ અથવા વનસ્પતિઓ દ્વારા વૈકલ્પિક ઉપચાર
(Alternatives therapies using herbs or botanicals)
આધુનિક જીવનશૈલીમાં પરિવર્તન
હાસ્ય કસરત,યોગ અને પ્રાણાયામ


કૃત્રિમ હોર્મોન દ્વારા ઉપચાર (Hormone Replacement Therapy)
એ કૃત્રિમ રીતે બનાવેલ એક કે તેથી વધુ સ્ત્રી હોર્મોનનો ઉપયોગ કરીને કરવામાં આવતી તબીબી સારવાર છે.
હોર્મોનની બનાવટો ગોળીઓ, જેલ , ત્વચામાં કે યોનિમાર્ગ માં દાખલ કરવાની ગોળીઓ, અને ઇન્જેક્શન તરીકે ઉપલબ્ધ છે.
કૃત્રિમ હોર્મોનથી થતી પ્રતિકુળ અસરોની ચિંતાને કારણે અન્ય વૈકલ્પિક ઉપચારની જરુર જણાઇ છે.
ફાયદા
જોખમો
મેનોપોઝની તકલીફોમાં રાહત
રક્તવાહિની ને લગતા રોગોના જોખમ માં ઘટાડો
અસ્થિસુષિરતામાં ઘટાડો
હૃદયરોગનો હુમલો
અંડાશયનું કેન્સર
સ્તનનું કેન્સર
અલ્ઝાઇમર ની બીમારી
લોહી ગંઠામણ


ફાઇટોઇસ્ટ્રોજન : મહત્ત્વ અને સ્રોત
ફાઇટોઇસ્ટ્રોજન એ સર્વ વ્યાપક, બિનસ્ટેરોઇડસ, કુદરતી રીતે છોડમાંથી મળી આવતુ ફિનોલીક ઘટક છે.
જેને "ખોરાકીય એન્ડ્રોજન" પણ કહેવાય છે, એની સંરચના માનવીય અંત : સ્રાવ (ઇસ્ટ્રોજન) ને મળતી આવે છે.
ફાઇટોઇસ્ટ્રોજન
આઇસોફ્લેવોન
કોમેસ્ટન્સ
લિગ્નાન
ડાઇડઝીન
જેનીસ્ટઇન
કોમેસ્ટોલ
એન્ટરોલેકટોન
એન્ટરોડાઇન
ગ્લાયસીટીન
ફાઇટોઇસ્ટ્રોજન વિવિધ આરોગ્ય વિકૃતિઓ જેવી કે,
• પ્રોસ્ટેટ, સ્તન, આંતરડા નું કેન્સર
•રક્તવાહિની ને લગતા રોગો (Cardiovascular diseases)
•મગજ કાર્ય વિકૃતિઓ (Brain function disorders)
• રજોનિવૃત્તિ -ની સમસ્યાઓ (Mneopausal problems)
• અસ્થિસુષિરતા (osteoporosis)
સામે રક્ષણાત્મક અસર ધરાવે છે.


ફાઇટોઇસ્ટ્રોજન યુક્ત ખોરાક
સોયાબીન અને તેની ઉત્પાદનો (Soybean and Its product)
અળસી (Flaxseeds)
મેથી (Fenugreek)
સૂરણ (Yam)
દાડમ (Pomegranate)
મસૂર (Lentils)
મગ (Green gram)
જવ (Barley, Oats)
ગાજર (Carrots)
ફૂદીના (Mint)
લસણ (Garlic)
ઓલિવનું તેલ (Olive oil)
જરદાળુ
સૂર્યમુખી બીજ (Sunflower seeds)
ઇસ્ટ્રોજન રિસેપ્ટર
estrogen receptors
ઇસ્ટ્રોજન
ફાઇટોઇસ્ટ્રોજન
ખોરાકમાંથી મળતા ફાઇટોઇસ્ટ્રોજન ની સંરચના શરીરમાં બનતા ઇસ્ટ્રોજન ને મળતી આવે છે, જેથી ફાઇટોઇસ્ટ્રોજન, જયારે શરીરમાં ઇસ્ટ્રોજનની ઊણપ વર્તાય, ત્યારે ઇસ્ટ્રોજનથી થતી અસર લાવવામાં મદદરૂપ થાય છે.





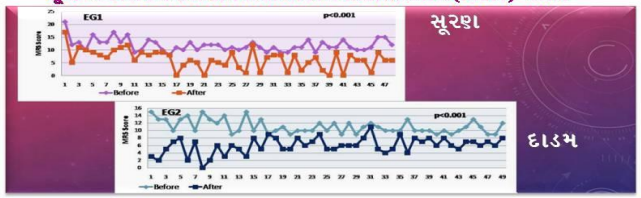
સૂર્ય નમસ્કાર

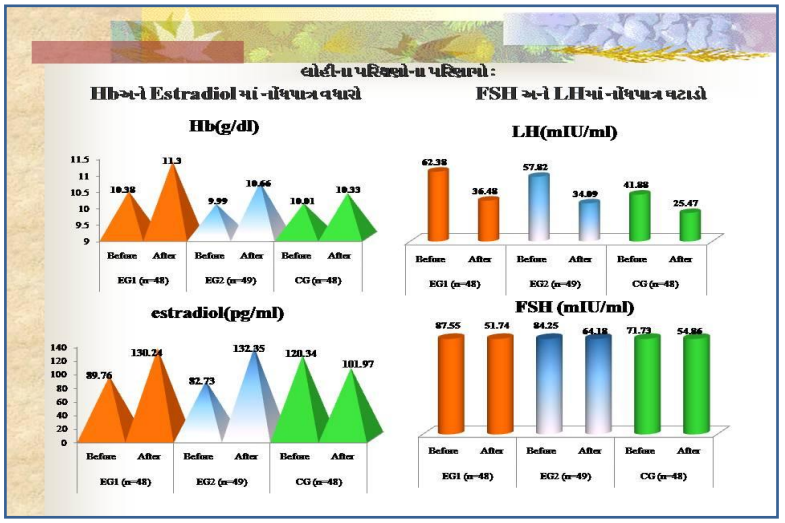
સ્ટ્રેચીંગ કસરતો

તાજેતરમાં કરવામાં આવેલ સંશોધન પ્રમાણે..

- દાડમ અને સૂરણના નિયમિત સેવનથી (n= ૧૫૦ સ્ત્રીઓ) પેરીમેનોપોઝ દરમિયાન થતી અસરો પર સંશોધન કરવામાં આવેલ, જેના તારણ અનુસાર દાડમ અને સૂરણ ના નિયમિત સેવનથી વિવિધ લાભદાયી જેવા કે માનસિક તકલીફો, યોનિમાર્ગની તકલીફોમાં તેમજ હૉર્મોનની માત્રામાં પણ નોંધપાત્ર સુધારો થાય છે. તદ્ઉપરાંત હાડ્ય કસરત, સ્ટ્રેચીંગ કસરત અને આધુનિક જીવનશૈલીમાં બદલાવ પણ મેનોપોઝ દરમિયાન થતી તકલીફોમાં રાહત મેળવવા મદદરૂપ થાય છે.

સૂરણ અને દાડમના સેવનથી મેનોપોઝ દરમિયાન થતી તકલીફોમાં (MRS) ઘટાડો





આભાર

- પ્રકાશક, આ પુસ્તિકામાં આપવામાં આવેલ માહિતીના સંકલનમાં મદદરૂપ દરેક સંદર્ભ (referances)ના આભારી છે.
- પ્રકાશક, ડિપાર્ટમેન્ટ ઓફ ફૂડ્સ એન્ડ ન્યુટ્રીશન,એમ.એસ.યુનિવર્સિટી; સંશોધનમાં ભાગ લેનાર સહભાગીઓ અને સંશોધનમાં આર્થિક સહાય બદલ યુજીસી ના આભારી છે.

અસ્વીકૃતિ

- આ પુસ્તિકામાં આપવામાં આવેલ માહિતી, સૂચના તથા તથ્યોનો ઉપયોગ વ્યક્તિના સ્વાસ્થ્ય સુધાર માટે કરવામાં આવે એ હિતાવહ છે. આ માહિતી દરેક વ્યક્તિને સંબંધિત તથા અનુકૂળ આવે એ જરૂરી નથી.
- આ પુસ્તિકામાં આપવામાં આવેલ માહિતી, સૂચના તથા તથ્યોને લઇને (કોઇ કાર્ય કરવાથી કે ન કરવાથી) કોઇ પણ પ્રકારની થતી હાનિ કે નુકસાન માટે પ્રકાશક કોઇ પણ જવાબદારી લેતા નથી.

References

- Division of Nutrition, Physical Activity, and Obesity, national Centre for Chronic Disease Prevention and Health Promotion. last updated: April 6, 2011
- http://www.cdc.gov/nutriiton/everyone/basics/vitamins/calcium.html
- The Diet Detective: How Nutrition and Diet Affect Bone Health. By Charles Stuart Platkin,2007
- http://www.active.com/nutrition/articles/the-diet-detective-how-nutriiton-and-diet-affect-bone-health
- Menopause Health club, Dr. Kala Shah
- Your Perimenopause Guidebook, by Stacey Colino
- Menopause-ek jankari (in Hindi) , By International Menopause Society, promoting education and research on all aspects's of adult women's health. www.imsociety.org
- http://menopausetreatment.com

In India, as like Iran (Noroozi et al., 2013), policies and programs of women's health promotion are specifically limited to specific issues such as pregnancy and family planning, and enough attention is not paid to other women's health needs, including the problems of menopausal transition period.

Physical, mental, psychological and social aspects need to be taken into consideration in developing appropriate programs. In addition, the tailored pre-, peri, postmenopausal educational intervention is required according to status, symptoms and severity of menopause. Overall, it is thought that it is necessary to make a nursing plan for health and wellbeing of middle-aged women in the menopause by developing and providing the health promotion program for them and minimizing their feeling of discomfort in the menopause as midlife women in the menopause had the low degree of performing menopausal management.

GENERAL OBSERVATIONS AND LIMITATION OF THE STUDY

Perimenopause begins with irregular menstrual cycle and the changes associated with this transition are due to changes in estradiol level. Women of Vadodara reported this transition at very young age; this could be due to some environmental factors, diet and lifestyle factors or genetic factors. This lower onset may adversely affect the health in later life. With our study design, it was not able to understand which factor plays a major role; the complexities were – most of women were not able to answer the onset age of menopause of her mother, the stress level and life style pattern were not similar among all women as the data was collected from a free living population. The most discouraging fact was majority of the women were not aware with the changes associated with this transition period and though they were suffering from various symptoms due to transition, was not taking any initiative or not realize the importance to consult a doctor. They considered this, as normal part of life. Therefore there is a need to create awareness and sensitize women about menopausal transition and its management. Among different types of menopausal symptoms, psychological symptoms like depression, irritability, anxiety, physical and mental exhaustion were affecting the most, in our study population. This would be obvious, as this is a time when women may experience fear of less attention by partner due to her less interest in sexual relation or so, children may go away for study or job purpose, their increasing independency etc. Hence, during this period, moral and social support and little more understanding given by other family members may play a major role health of quality of middle age women.

The use of phytoestrogen for postmenopausal women has been well studied for western population. In this study, we have identified and quantified phytoestrogen form four foods – fenugreek seeds, tuber of elephant foot yam, flaxseeds and pomegranate seeds, which are locally available, acceptable and affordable by our population. HPLC analysis was used for this analysis; this gives an approximation for the type and quantity of components present in samples. For better identification and quantification, Mass Spectroscopy is required; but the cost was the limitation for us.

At baseline, general hormonal and health profile of women (n=150) showed 79% women were anemic, hemoglobin level did not found any effect on thyroid hormone levels, serum FSH, LH or estradiol levels. The experiences of menopausal symptoms were also not much vary among the normal or anemic women. We found a significant interrelation between BMI and serum estradiol level and WHI with serum LH and estradiol in our population. This showed a direct effect of estradiol on nutritional status and abdominal obesity at physiological level.

The phytoestrogen supplementation for 45 days, showed an improvement in BMI and WHI of women. This reflected a structural similarity of phytoestrogen may helpat mRNA level to prevent adipogenesis and weight reduction. We also observed a significant change in serum FSH, LH and estradiol level after phytoestrogen supplementation.Such changes at hormone levelscould help to get a significant relief in MRS. This supports the potential effect of phytoestrogen at MRS and serum gonadotropins and estradiol level during perimenopause. The alternative approach – nutritional and physical health education also showed a significant improvement at MRS score but not able to bring the change at hormone levels. We also faced few limitations in interpretation of the

findings - as women were not able to answer their menstrual cycle pattern, as well as the pattern of irregularity and therefore the level of gonadotropins in population could not be standardizedto obtain optimal results with phytoestrogens or its impact.