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TABLE OF CONTENTS

Editorial

1. What Impact for Sex Difference on Immune Thrombocytopenic Purpura? e1-e3
– Emmanuel Andrés*

Editorial

2. The Stigma of Rape: Gendered Victimization e4-e5
– L. N. Suman*

Editorial

3. The Zika Virus has Arrived in the United States e6-e7
– Susan Ricci*

Research

4. Measuring Climacteric Symptoms: A Community based Study among
Lotha Females of Nagaland 1-7
– Peteneinuo Rülü, Meenal Dhall and Satwanti Kapoor*

Opinion

5. The Current State of Professional Midwives in Japan and their Traditional
Virtues 8-10
– Masafumi Koshiyama*, Yumiko Watanabe, Natsuko Motooka and Haruko Horiuchi

Editorial

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What Impact for Sex Difference on Immune Thrombocytopenic Purpura?

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KEYWORDS: Idiopathic thrombocytopenic purpura; Primary immune thrombocytopenia; Gender female; Male; Clinical manifestations; Score.

Despite the progress in medicine the impact of gender on many diseases remains unknown or unstudied. In this context, it seemed appropriate to us, with a bit of provocation, to study the impact of gender on Immune Thrombocytopenic Purpura (ITP).

ITP, currently also known as primary immune thrombocytopenia, is an autoimmune disorder that results in acute or chronic thrombocytopenia and that may potentially lead to a life-threatening hemorrhagic event.¹

Major advances in our understanding of the pathophysiology of ITP have been done last years (evidence of anti-platelet antibodies and the relative failure of bone marrow platelet production),² but the diagnosis of ITP still is based on exclusion.¹

While ITP in childhood is usually an acute, self-limiting condition (the thrombocytopenia is transient and recovers spontaneously despite an initially severe presentation), ITP is more often a chronic disease in adults (at least 30% of cases) with an insidious onset requiring multiple therapeutic approach.¹

ITP mainly occurs in young adults, particularly women in their third or fourth decade, with an overall female to male ratio of 3-4 to 1. These figures suggest that sex hormones, as in other immune disorders (systemic lupus, multiple sclerosis, etc.) may play a role in the susceptibility to ITP.³ In addition to having an impact on the immune system, sex hormones may also alter the clinical picture and response to therapy.

In recent years, it has become clear that women and men may differ for drug response. There is an increasing recognition on the role of sex hormones on pharmacokinetics and pharmacodynamics as mechanism accounting for sex differences in drug effects. The available evidence suggests that sex hormones influence drug absorption, distribution, metabolism, pharmacodynamics, and adverse effects. For instance, many cardiovascular drugs are metabolized by enzymes of the cytochrome system, which is more expressed in females than in males, showing sex differences in drug response. A line of evidence also exists that posits that genetic variation among different genders may be responsible for the variability in therapeutic response.

We have previously reported such a gender-related analysis in 225 consecutive cases of established ITP followed up over a period of 1.7 to 112 in the Strasbourg University Hospital (Strasbourg, France).⁴

The analysis of the data revealed significant statistical differences between female and male for: 1) the bleeding score: 13±6.3 in females *versus* 8.4±4.1 in males ($p=0.03$); 2)

the presence of a documented anemia: 7 % in females *versus* 4.3 % in males ($p=0.04$); and 3) the detection of antinuclear and/or antiphospholipid antibodies: 64.7 % *versus* 35.3 % ($p<0.02$) (Table 1). For the first 2 parameters, the difference may be related to the presence of meno- and/or metrorrhagia and hematuria in female patients.

	Female patients (n=156)	Male patients (n=69)
Mean age at initial diagnosis of ITP	45.2±24.7 years (range, 18-82)	47.8±21.4 years (range, 15-71)
Presentation of ITP:		
• Thrombocytopenia revealed by routine full blood count	82(52.5%)	35(50.7%)
• Thrombocytopenia revealed by a bleeding diathesis	74(47.5%)	34(49.3%)
Mean bleeding score from Khellaf et al.	13±6.3* (range, 3-32)	8.4±4.1* (range, 3-17)
Mean platelet count	44.5±19x10 ⁹ /l (range, 1-131)	38.4±14x10 ⁹ /l (range, 1-118)
Presence of a potential life-threatening platelet count (platelet count <10x10 ⁹ /l)	28(17.9 %)	11(15.9 %)
Mean hemoglobin level	12 g/dl (range, 8.2-13.6)	12.6 g/dl (range, 9.1-14.7)
Presence of anemia (hemoglobin level <12 g/dl)	11(7%)*	3(4.3%)*
Detection of antinuclear antibodies and/or antiphospholipid antibodies (n=140)	22(64.7%)*	12(35.3%)*

*statistically significant difference.

Table 1: Gender-related analysis of clinical and biological presentations in 225 patients with idiopathic thrombocytopenic purpura (ITP).

No statistically significant difference was found regarding outcome for these 225 patients in relation to their gender (Table 2).

	Female patients (n=156)	Male patients (n=69)
Patients with CR or PR		
- Spontaneous response or after first-line therapy (steroids, IgIV)	56(35.9%)	26(37.7%)
- After second-line therapy (splenectomy, rituximab)	44(28.2%)	21(30.4%)
Patients with chronic ITP requiring long-term drug use (steroids, danazol, etc.) due to recurrent and chronic bleeding and/or low platelet counts	39(25%)	19(27.5%)
Patients with chronic ITP and PR or F [7] managed with a 'wait-and-see' policy and punctual treatment	14(9%)	6(8.7%)

IgIV: intravenous immunoglobulins. CR: complete response (platelet count >150x10⁹/l after treatment). PR: partial response (platelet count of 50 to 150x10⁹/l or platelet levels twofold higher after treatment if the initial platelet count was <50x10⁹/l). F: failure.

Table 2: Gender-related analysis of outcomes in 225 patients with idiopathic thrombocytopenic purpura (ITP).

An abundance of recent research indicates that there are multiple differences between males and females regarding both the normal physiological processes and the pathophysiology of disease. Studies have addressed sex-based differences in the physiology and pathophysiology of the cardiovascular, musculoskeletal, and immune systems as well as the mechanism of action of sex steroid hormone actions on nonreproductive tissues.⁵

Thus, as is the case for several other autoimmune disorders, the role of patient gender in the course and outcome of ITP should be considered.

A strikingly common feature observed in many autoimmune diseases in both humans and animal models is that females are highly susceptible to autoimmune conditions as compared with males-regardless of the differences in disease pathology.⁵ This is the case in several documented studies of ITP.¹

In several animal models, estrogens promote, whereas androgens abrogate, B-cell-mediated autoimmune diseases.⁵ Estrogens are able to influence the immune response *via* several mechanisms, but recently, they have been shown (along with other sex hormones) to largely exert their effects on immune effector cells, modulating the expression and production of several cytokines.⁵ This is a potential explanation for the efficacy of danazol in ITP.⁴

Thus to date, the impact for sex difference on immune thrombocytopenic purpura or on primary immune thrombocytopenia is not known.

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Editorial

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The Stigma of Rape: Gendered Victimization

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The problem of rape is as old as civilization and it is a universal concern of great magnitude. Rape is classified as a violent crime in all nations and attracts strong penal action. This however has not deterred sexual offenders, and statistics related to rape indicate that it continues to traumatize not only women but men and children also. In India, rape is more common against girls and women. The proportion of crime committed against women against all types of crime in 2012 was 9.40% according to the National Crime Records Bureau (NCRB).¹ Of this, 1% was rape and in 98.20% of cases, the offenders were known to the victims. It is likely that the figures may be much higher as many victims do not report the crime to the police due to fear of stigma and its consequences.

In patriarchal countries such as India, the offender is rarely punished or shamed. Politicians and other public figures in India often dismiss rape as a forgivable offence with one political leader recently describing rape as an understandable act since 'boys will be boys'. Others have blamed women for the act and have dismissed accusations of rape as only 'mistakes committed by men'. Some public figures have recommended punishing the victim also for the crime.² Laws are rarely implemented even when the victim and her family muster the courage to file a complaint. The police also discourage the victim from registering a complaint as it would sully her image in society. For instance, the police refused to register a complaint of rape when a minor victim along with her mother went to the police station to report the crime. The police advised the mother against filing a complaint as her daughter's reputation would be ruined.³ As a result of such attitudes; men go scot free after committing the criminal act, adding to the misery of the victims. Even in cases where a complaint is registered, girls and women are re-traumatized during medical examination when doctors use the humiliating 'two finger test' to confirm rape instead of more advanced medical procedures.⁴

While little or no stigma is attached to a male rapist, girls and women who have been raped are victimized by family members, friends and society for bringing shame and dishonour to the family. An unmarried girl, who has been raped, is considered to be unfit for marriage as she is no longer 'pure'. A rape victim embodies the living dead since she will always have to live with social stigma. In some cases, the victims have been forced to marry the rapist as a compromise and it has even been recommended by a high court judge as a solution for the victim.⁵ The reputation of girls and women in India is defined in terms of 'sexual purity' which has to be protected at all costs. Failure to do so, invites wrath even if the victim has suffered severely at the hands of the perpetrator. Loss of virginity through rape or 'defilement' of a married woman by a rapist is often considered to be a sin that has to be atoned for by the victim. Further, the victim's parents or spouse are also blamed for not 'bringing up the girl with adequate moral standards' or 'not having control over one's wife'. The family members in turn blame the victim for their plight leading to the burden of shame and guilt in the victim. In many instances, family members tell the victim that they would be better off if she were dead. Thus, the emotional and social costs of the crime are enormous for the victim, leading to further traumatization. Hence, rape is often described by women as an experience 'worse than death'.

Two examples will serve to illustrate the nature of punishment and victimization meted out to victims of rape in India. The subjects of the examples were part of a larger study on

loss, trauma and suicidal ideation among women living in a shelter published elsewhere.⁶ In the first case, an 18-year old girl was raped by a boy who was employed in the local post office, where her father also worked, when he found her alone at home. The mother was devastated and her father was infuriated when they were informed about the incident. The loss of face in society was too much for the father to bear and he decided to inform the victim to leave the house. In spite of the entreaties of the mother, the girl was forced to leave the house with instructions to 'never come back' and no complaint was filed against the boy. The girl made her way to the shelter with the help of well-wishers of the family.

In the second case, a 21 year old young woman sought refuge in the shelter as she did not want to live with her paternal aunt's family with whom she was staying after her father's death when she was six years old. When she was 20 years old, she was raped repeatedly by her paternal cousin. When she informed her aunt, she was criticized for lying which emboldened her cousin to continue the abuse. The victim became pregnant after a few months and her aunt was forced to acknowledge the truth. She however ensured that the matter remained a family secret and managed to take the victim to another town till the delivery of the baby, after which the baby was given away to an orphanage. Subsequently, the victim decided not to go back with her aunt and made plans to live in a shelter home.

The examples indicate that the authority of the head of the household cannot be questioned and that close female relatives may also not be supportive when their family's reputation is at stake. The physical and emotional suffering of the victims is considered to be of no consequence. Their rights are violated and they often have no one to turn to as they are ostracized or betrayed by their own family members. The girls are sacrificed at the altar of 'family honour' and the agony and trauma of their mothers and siblings are very often not addressed. The stigma increases manifold if the woman becomes pregnant following rape and gives birth to a child. In such cases, the stigma also gets attached to the child, condemning it to a life of rejection and hostility. Further, if girls and women are abandoned by their families after rape, they become potential victims of sex traffickers and they will be doomed to a life of forced prostitution. Hence, social and cultural attitudes towards rape and victims of rape have to be addressed to protect girls and women against a vicious cycle of victimization. Barriers to reporting the crime and obtaining justice have to be minimized and the law has to be enforced stringently against the offender. This requires sustained and committed efforts by various sections of the society as well as law enforcers.

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Editorial

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The Zika Virus has Arrived in the United States

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Current media broadcasts have been reporting about the rapidly spreading outbreaks of the Zika virus now identified in South and Central America, as well as Mexico, the Caribbean, Puerto Rico and now in the United States. Focal activity of the *Aedes* species mosquito that transmits the Zika virus to humans through its bite, has been reported in South Florida. Prior to 2007, Zika was not reported outside of Africa and Asia, but since it was discovered recently in Brazil in 2015, the virus has swiftly spread across several continents.

Zika is transmitted to humans by an infected mosquito bite during a blood meal by the *Aedes* species. They are also responsible for the transmission of dengue fever and chikungunya viruses. Unlike other species of mosquitos, the *Aedes* mosquitos often hide indoors and in shaded areas and are aggressive daytime biters, thus making it very challenging to prevent the spread of infections.¹ Transmission occurs perinatally, in utero, sexual contact, blood transfusions and bodily fluids. To date, transmission through breastfeeding has not been reported, but limited studies are available, therefore absolute conclusions about modes of transmission cannot be determined at this time.²

Only about 1 in 5 people infected with Zika virus are symptomatic. In people who do experience symptoms, they will occur between 3 and 12 days after being bitten by an infected mosquito and will last between 2 and 7 days. The most common symptoms are fever, maculopapular rash, headache, arthralgia, non-purulent conjunctivitis, myalgia, retro-orbital pain and vomiting.³ Severe disease requiring hospitalization are uncommon. As in the case of other viral illnesses, once infected, individuals are protected from future infection.

Much focus has been on women that contract the Zika virus while pregnant. The Zika virus has been linked to microcephaly in newborns born to those infected. Microcephaly is a neurologic condition in which the newborn's head is smaller and the result of abnormal brain development in utero. In addition to microcephaly, there is some evidence that the Zika virus is also linked to miscarriage and stillbirth.⁴

Testing for Zika currently involves blood and urine specimens. Polymerase chain reaction (PCR) can be used to detect viral ribonucleic acid (RNA) in serum and urine during the first week of illness and in urine alone for samples collected 1 to 3 weeks after illness onset. Both Zika virus PCR and antibody testing are commercially available.

Healthcare professionals play a key role in disseminating information to the public and must remain up-to-date with Centers for Disease Control and Prevention (CDC) and World Health Organization (WHO) recommendations. Clinicians should be educated about the hallmark signs and symptoms of Zika virus and advise their clients about precautions to take. Pregnant women should protect themselves from mosquitoes and avoid traveling to regions where Zika virus is present. In addition, men who travel to infected areas should use condoms to protect their sexual partners. The use of Environmental Protection Agency (EPA) registered insect repellent can help prevent mosquito bites in all people.

The CDC has released clinical guidelines for the evaluation, clinical manifestations, diagnosis, and treatment of the Zika virus for all professionals. As it currently stands, there is no vaccine or prophylactic treatment available, but the first vaccine is in the pipeline.² Healthcare professionals should educate their clients on infection control, personal protection, and prevention against this illness. These simple precautions may help prevent people from contracting the virus as well as the potential birth defects that could result.

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Research

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Measuring Climacteric Symptoms: A Community based Study among Lotha Females of Nagaland

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ABSTRACT

Background: The overall health and well-being of the mid-aged women has become a major public health concern around the world. Before and after the onset of menopause, women experience physical or psychological symptoms which affect the overall health leading to decrease in Quality of Life (QoL).

Objective: To measure the climacteric symptoms and risk factors.

Materials and Methods: Cross-sectional data was collected on a sample of 202 adult females. Data was collected by multi-stratified sampling method. The subjects ranged in age from 35-60 years. Data was collected on socio-demographic aspects, health, quality of life and physiological parameters.

Results: The mean and median age of the subject was 48.3 ± 7.6 and 49 years respectively. The mean and median age of pre-menopausal females was found to be 41.2 ± 4.6 and 41 years respectively and of post-menopausal females it was 54.2 ± 3.5 and 54 years respectively. Among pre-menopausal females higher percentage of headache was found whereas among post-menopausal females sexual dysfunction was found to be the most prevalent symptom. Highly significant values were found for all the menopausal symptoms in clusters, sub-clusters and total Greene score among post-menopausal females. For the severity of menopausal symptoms, post-menopausal females who had low quality of life were found to be at higher risk for developing all the menopausal symptoms.

Conclusion: In the present study, factors like family size, health status and age at menarche line were found to be the risk factors for menopausal symptoms. Females having low quality of life were also seen to have higher menopausal symptoms.

KEYWORDS: Menopause; Quality of life; Menopausal symptoms; Nagaland; Lotha females.

ABBREVIATIONS: QoL: Quality of Life; FMP: Final Menstrual Period; WHO: World Health Organization; WHOQOL: The World Health Organization Quality of Life; GCS: Greene Climacteric Scale; CI: Confidence Interval.

INTRODUCTION

Menopause is the permanent cessation of menstruation resulting from the loss of follicular activity in the ovaries. It is a stage when the menstruation cycle stops for longer than 12 months and there is a drop in the estrogen and progesterone, the two important hormones in the female body.¹ 'Menopause' was derived by a French physician in 1821, from the Greek word 'menos' for 'month' and 'pause' for 'to stop'.² The age at which menopause occurs differs individually, culturally and geographically. Age at menopause is calculated in years by the Final Menstrual Period (FMP) in women's life. The age at menopause may be obtained by periodically asking them about the absence or presence of menstrual cycles or by asking them to recall their age at the time of last menstrual period.³

Even before the onset of menopause, menopausal symptoms may occur and their effect differs individually. Some individuals may not find it bothersome while other might se-

verely be affected causing difficulties to perform daily activities. The menopausal transition is a function of progressive decline in ovarian follicular population and reduced steroidogenic capacity of ovarian stroma, as such it represents ovarian senescence.⁴ During the menopausal transition, physiological as well as morphological changes occur. A variety of physiological changes takes place in the body and some of these are result of cessation of ovarian function and related menopausal events, others are function of ageing process.¹ Little distinction has been made between symptoms that result from a loss of ovarian functions, from the ageing process or from the socio-environmental stresses of mid-life years.¹

Menopause related symptoms have been studied extensively in western countries but very less data is available from developing countries, especially South East Asia.⁵ Based on various researches World Health Organization (WHO)¹ classified the symptoms of menopause into vasomotor symptoms, urogenital atrophy, irregular menstruation and other problems. Most of the women with the onset of menopause suffer from various symptoms which may or may not be related to menopause. The various symptoms of menopause have been categorized by scholars and researchers in their in-depth study and for the association between the severities of those symptoms with menopause. To study the effect and severity of these symptoms various standardized questionnaires have been developed and extensively used for the study. The various menopausal symptoms experienced by the subjects are mostly classified into various categories like, psychological, somatic, vasomotor, sexual dysfunction etc.

In North-East India very few studies have been done on menopause and no published literature has been found among Lotha females. Thus, the present study focuses on the various climacteric symptoms and their risk factor using the Greene climacteric scale among adult Lotha females of Nagaland.

MATERIALS AND METHODS

The present study was carried out among adult Lotha females of Wozhuro range under Wokha district, Nagaland. This group of people belong to Tibeto-Burman family, followed clan exogamy. Their primary occupation is shifting cultivation. They belong to one of the major tribes in Nagaland.

For the collection of data an exclusion criteria was set and those subjects who were pregnant, unmarried and have undergone induced menopause were excluded from the study. Data was collected on 202 females of which 111 females were post-menopausal i.e. stopped menstruating and 91 females were pre-menopausal i.e. they were still menstruating. Cross-sectional data was collected by using multi-stratified sampling. A structured proforma was prepared to collect data on socio-demographic parameters like age, educational status, house type, family size, occupation etc. and on reproductive history like age at menarche, age at marriage, age at menopause etc. The quality

of life among the subjects was also analyzed using The World Health Organization Quality of Life (WHOQOL)⁶ questionnaire developed by WHO in 1996 in an attempt to develop a quality of life assessment that would be applicable cross-culturally. The WHOQOL consist of various questions with scores ranging from 1-5 based on the severity and the median value of the total score was taken after which the values below the median score was labelled as low quality of life and the values above the median score was labelled as high quality of life.

There are various questionnaire developed for assessing the severity or the type of symptoms associated with menopause and are being used widely by researchers for studying menopausal symptoms.

In the present study, the Greene Climacteric Scale (GCS) have been used to assess the menopausal symptoms experienced by the subjects. The Greene Climacteric Scale⁷ provides a brief measure of menopausal symptoms and has classified the symptoms into psychological symptoms, physical or somatic symptoms and vasomotor symptoms which can be used to assess changes in different symptoms, before and after menopause. The scale consist of 21 questions with four point rating scale based on the severity: not at all (0); a little (1); quite a bit (2); extremely (3).

In psychological symptoms it includes 11 symptoms such as heart beating quickly or strongly, feeling tense or nervous, difficulty in sleeping, excitable, attacks of anxiety and panic, difficulty in concentrating, feeling tired or lacking in energy, loss of interest in most things, feeling unhappy or depressed, crying spells and irritability, the somatic or physical domains include symptoms such as feeling dizzy or faint, pressure or tightness in the head, parts of the body feel numb, headaches, muscle or joint pains, loss of feelings in the hands or feet, breathing difficulties, and the vasomotor domain include symptoms like hot flushes, night sweats and lastly sexual dysfunction.

Analysis was performed using Statistical software package SPSS version 17. Multinomial logistic regression was used to analyze the severity of the menopausal symptoms with socio-demographic and reproductive as well as nutritional status among post-menopausal females. In the present study, purpose of the study was explained and written informed consent was obtained from all the participants before starting the study. Ethical clearance was taken prior to start the work from Departmental ethical committee.

RESULTS

The mean and median age of the present study was found to be 48.3 ± 7.6 and 49 years respectively (Table 1). The mean and median age of pre-menopausal was found to be 41.2 ± 4.6 and 41 years and among post-menopausal females were 54.2 ± 3.5 and 54 years respectively. Table 2 describes the mean, standard deviation and t-test values of menopausal symptoms us-

Age (years)	Mean±SD	Median
Total population	48.3±7.6	49
Pre-menopausal females	41.2±4.6	41
Post-menopausal females	54.2±3.5	54

Table 1: The age of Nagaland females.

Psychological symptoms	Mean±S.D (%)			t-test
	Total	Pre-menopause	Post-menopause	
Heart beating quickly or strongly	0.29±0.47(28.2)	0.24±0.45(10.3)	0.33±0.49(17.8)	-1.36
Feeling tense or nervous	0.64±0.50(62.8)	0.57±0.51(25.2)	0.69±0.48(37.6)	-1.73
Difficulty in breathing	1.28±0.91(55.9)	0.88±0.91(23.2)	1.61±0.77(47.0)	-6.15***
Excitable	0.15±0.35(14.8)	0.11±0.31(4.9)	0.18±0.38(9.9)	-1.39
Attacks of anxiety, panic	0.25±0.43(24.7)	0.16±0.37(7.4)	0.32±0.46(17.3)	-2.49*
Difficulty in concentrating	0.93±0.66(74.2)	0.75±0.66(28.2)	1.08±0.63(46.6)	-3.65***
Feeling tired or lack in energy	1.69±0.49(67.3)	1.52±0.54(22.2)	1.83±0.40(45.0)	-4.68***
Loss of interest in most things	0.85±0.58(74.7)	0.62±0.55(26.2)	1.05±0.52(48.5)	-5.62***
Feeling unhappy or depressed	1.04±0.43(92.5)	1.02±0.36(42.5)	1.06±0.49(50.0)	-0.66
Crying spells	0.29±0.45(29.2)	0.32±0.46(14.3)	0.27±0.44(14.8)	0.75
Irritability	0.16±0.37(16.3)	0.18±0.38(7.9)	0.15±0.36(8.4)	0.43
Feeling dizzy or faint	0.27±0.45(26.7)	0.15±0.36(6.9)	0.37±0.50(19.8)	-3.42***
Pressure or tightness in the body	0.65±0.57(59.9)	0.52±0.58(21.2)	0.76±0.54(38.6)	-3.02**
Parts of the body feel numb	0.23±0.45(21.1)	0.12±0.32(5.4)	0.32±0.52(15.8)	-3.08**
Headaches	1.53±0.52(94.0)	1.43±0.54(44.0)	1.62±0.48(54.9)	-2.66**
Muscle and joint pains	1.17±0.70(82.1)	0.85±0.69(30.1)	1.44±0.59(51.9)	-6.52***
Loss of feeling of hands or feet	0.15±0.37(14.8)	0.05±0.22(2.4)	0.23±0.44(12.3)	-3.47***
Breathing difficulty	0.20±0.39(19.8)	0.12±0.32(5.4)	0.26±0.44(14.3)	-2.51*
Hot flushes	0.74±0.79(51.9)	0.43±0.74(12.3)	0.99±0.74(39.6)	-5.33***
Sweating at night	0.76±0.76(55.9)	0.57±0.79(17.3)	0.92±0.71(38.6)	-3.27***
Sexual dysfunction	2.64±0.74(97.2)	2.22±0.94(42.5)	2.99±0.09(54.9)	-8.59***

*** $p < 0.001$, ** $p < 0.01$, * $p < 0.05$

Table 2: Menopausal symptoms based on Greene Climacteric Scale (GCS).

ing the Greene Climacteric Scale. Scores in all the menopausal symptoms except crying spells and irritability showed increase among post-menopausal females as compared with pre-menopausal females. The difference between the two groups were found to be statistically significant in symptoms such as difficulty in breathing ($p < 0.001$), attacks of anxiety, panic ($p < 0.05$), difficulty in concentrating ($p < 0.001$), feeling tired or lacking in energy ($p < 0.001$), loss of interest in most things ($p < 0.001$), feeling dizzy or faint ($p < 0.001$), pressure or tightness in the body ($p < 0.01$), parts of the body feeling numb ($p < 0.01$), headaches ($p < 0.01$), muscle and joint pains ($p < 0.001$), loss of feelings of hands and feet ($p < 0.001$), breathing difficulty ($p < 0.05$), hot flushes ($p < 0.001$), sweating at night ($p < 0.001$) and sexual dysfunction ($p < 0.001$).

Most prevalent symptoms experienced by pre-menopausal females was headache followed by sexual dysfunction and feeling unhappy or depressed and among post-menopausal females, it was headache and sexual dysfunction followed by

muscle and joint pain. In the total score, the most prevalent menopausal symptom was sexual dysfunction followed by headache and feeling unhappy or depressed. Symptoms like muscle and joint pain, loss of interest in most things and difficulty in concentrating also showed high prevalence.

The cluster, sub-cluster and total Greene score was also calculated where the mean, standard deviation and t-test was taken to analyze the difference between the two groups (Table 3). This result showed that the cluster and sub-cluster such as psychological, anxiety, depression, somatic, vasomotor, sexual dysfunction and total Greene score was found to be more among post-menopausal females as compared with pre-menopausal females and this difference was found to be highly significant ($p < 0.001$).

Multinomial logistic regression was calculated at 95% Confidence Interval (CI) among post-menopausal females to see the effect of demographic, health, lifestyle indicators on the se-

Variables	Mean±S.D		t-test
	Pre-menopause	Post-menopause	
Psychological	6.4±3.33	8.6±3.20	-4.799***
Anxiety	2.7±2.10	4.2±2.09	-5.054***
Depression	3.6±1.58	4.3±1.43	-3.348***
Somatic	3.2±2.12	5.0±2.55	-5.243***
Vasomotor	1.0±1.49	1.9±1.32	-4.578***
Sexual dysfunction	2.2±0.94	2.9±0.09	-8.591***
Total Greene Score	12.8±6.58	18.4±5.90	-6.426***

***p<0.001, **p<0.01, *p<0.05

Table 3: Cluster, sub-cluster and total Greene score according to menopausal status.

Variables	Psychological (>8)	Anxiety (>3)	Depression (>4)	Somatic (>5)	Vasomotor (>2)	Total Greene Score (>18)
Age						
≥54 years	2.3(0.9-6.2)	0.4(0.1-1.2)	0.4(0.1-1.1)	1.2(0.5-3.0)	1.0(0.4-2.5)	1.4(0.5-3.6)
<54 years †						
Education						
≤ primary class	0.9(0.2-3.1)	0.8(0.2-2.7)	0.9(0.2-3.2)	1.3(0.4-4.0)	0.8(0.2-2.6)	0.8(0.2-3.1)
≥ middle class †						
Family size						
≥6	1.2(0.5-3.1)	0.8(0.3-2.1)	1.8(0.7-4.5)	0.5(0.2-1.3)	2.5(1.0-6.4)*	0.7(0.3-1.8)
<6 †						
Health status						
Average	35.3(3.9-314.6)***	1.5(0.3-6.8)	-	3.6(0.8-15.4)	4.6(1.1-18.4)*	-
Poor	40.9(3.5-467.7)**	1.6(0.2-11.1)	-	20.1(2.6-155.9)*	7.2(1.2-44.1)*	-
Fit †						
Age at menarche						
<14	1.5(0.6-3.9)	1.4(0.5-3.5)	1.2(0.5-3.1)	1.3(0.6-3.1)	3.0(1.2-7.3)**	2.7(1.1-6.7)*
≥14 †						
Quality of life						
Low quality of life	8.6(3.4-21.5)***	4.6(1.6-13.0)**	1.6(0.5-5.0)	1.6(0.5-5.0)	3.2(1.3-7.5)**	6.3(2.5-16.1)***
High quality of life †						
Body mass index						
Underweight	1.4(0.4-4.0)	0.9(0.3-2.7)	1.6(0.5-4.3)	1.6(0.6-4.2)	0.6(0.2-1.5)	1.8(0.6-5.1)
Overweight	0.4(0.1-3.4)	0.3(0.04-2.4)	0.6(0.1-8.5)	2.1(0.3-14.8)	0.5(0.1-5.0)	0.9(0.1-7.6)
Normal †						

*p<0.05, **p<0.01, ***p<0.001

†Reference category

Table 4: Demographic, health, lifestyle indicators as a risk factor for severity of menopausal symptoms among post-menopausal females.

verity of menopausal symptoms. From Table 4, it was observed that females with age of ≥54 years were 2.3 times more at risk of developing psychological symptoms >8 than those females who were to <54 years of age, 0.4 times more risk of developing anxiety >3, 0.4 times more risk for developing depression >4, 1.2 times more risk of developing somatic symptoms >5, 1.0 times more risk of developing vasomotor symptoms >2 and 1.4 times more for total Greene score >18 and the risk factor was non-significant. In education qualification when compared with those ≤primary and ≥middle class, subjects who attained only ≤primary class were 0.9 times more risk for developing psychological symptoms >8, 0.8 times more risk for anxiety >3, 0.9

times more risk for depression >4, 1.3 times more risk for somatic symptoms >5, 0.8 times more risk for vasomotor symptoms >2 and 0.8 times more risk for total Greene score >18. Those subjects who had ≥6 members in a family were 1.2 times more at risk for developing psychological symptoms >8 than those with ≤6 members, 0.8 times more risk for developing anxiety >3, 1.8 times more risk for depression >4, 0.5 times more risk for somatic symptoms >5, 2.5 times more risk for developing vasomotor symptoms >2 (p<0.05) and 0.7 times more risk for total Greene score >18. The self-perceived health status of post-menopausal females showed that subjects with average health status were 35.3 times more risk for psychological symptoms >8

($p < 0.001$), 1.5 times more risk for anxiety > 3 , 3.6 times more risk for somatic symptoms > 5 , and 4.6 times more risk for vasomotor symptoms > 2 ($p < 0.05$) than those subjects with good/fit health status. For depression > 4 and total Greene score > 18 no result and difference was observed. For post-menopausal subjects with poor health status, they were 40.9 times more at risk for psychological symptoms > 8 ($p < 0.01$), 1.6 times more at risk for anxiety > 3 , 20.1 times more at risk for somatic symptoms > 5 ($p < 0.05$) and 7.2 times more at risk for vasomotor symptoms > 2 ($p < 0.05$) than those with good/fit health status. For depression > 4 and total Greene score > 18 no result was observed.

The age at menarche at ≤ 14 years were 1.5 times more at risk for psychological symptoms > 8 , 1.4 times more at risk for anxiety > 3 , 1.2 times more at risk for depression > 4 , 1.3 times more at risk for somatic symptoms (> 5), 3.0 times more at risk for vasomotor symptoms > 2 ($p < 0.01$) and 2.7 times more risk for total Greene score > 18 ($p < 0.05$) than those with age of ≥ 14 years. The quality of life was also assessed and found that post-menopausal subjects with low quality of life were 8.6 times more at risk for psychological symptoms > 8 ($p < 0.001$), 4.6 times more risk for anxiety > 3 ($p < 0.01$), 1.6 times more risk for depression > 4 , 3.4 times more risk for somatic symptoms > 5 ($p < 0.01$), 3.2 times more at risk for vasomotor symptoms > 2 ($p < 0.01$) and 6.3 times more risk for total Greene score > 18 ($p < 0.001$) than those with good quality of life. In Body Mass Index (BMI), subjects who were underweight were 1.4 times more at risk for psychological symptoms > 8 , 0.9 times more at risk for anxiety > 3 , 1.6 times more at risk for depression > 4 , 1.6 times more for somatic symptoms > 5 , 0.6 times more at risk for vasomotor symptoms > 2 and 1.8 times more for total Greene score > 18 . Those subjects who were overweight were found to be 0.4 times more at risk for psychological problems > 8 , 0.3 times more at risk for anxiety > 3 , 0.6 times more at risk for depression > 4 , 2.1 times more at risk for somatic symptoms > 5 , 0.5 times more for vasomotor symptoms > 2 and 0.9 times more for total Greene score > 18 . The risk factor of BMI among underweight and overweight post-menopausal females when compared with normal post-menopausal females were found to be non-significant for all the menopausal symptoms.

DISCUSSION

In developed countries, the climacteric affecting women from a bio-psycho and social point of view has extensively been studied.⁸ Symptoms at midlife are associated with a wide range of socio-demographic, lifestyle and health measures.⁹⁻¹¹ In the present study, scores in all the menopausal symptoms except crying spells and irritability were more in post-menopausal females as compared with pre-menopausal females. This findings agrees with the studies reported by various researchers.¹²⁻¹⁴ The difference between the two group was found to be statistically significant in symptoms such as difficulty in breathing, attacks of anxiety, panic, difficulty in concentrating, feeling tired or lacking in energy, loss of interest in most things, feeling dizzy or faint, pressure or tightness in the body, parts of the body feeling numb, headaches, muscle and joint pains, loss of feelings

of hands and feet, breathing difficulty, hot flushes, sweating at night and sexual dysfunction. Barentsen et al¹⁵ found higher and statistically significant symptoms among post-menopausal women such as feeling tense or nervous, difficulty in sleeping, attacks of panic, loss of interest in most things, irritability, feeling dizzy or faint, pressure or tightness in head or body, parts of body feeling numb, muscle or joint pain, loss of feeling in hands or feet, hot flushes, night sweats and sexual dysfunction.

Most prevalent symptoms experienced by present pre-menopausal females was headache followed by sexual dysfunction and feeling unhappy or depressed and among post-menopausal females, headache and sexual dysfunction were most prevalent followed by muscle and joint pain. In the total score, the most prevalent menopausal symptom was sexual dysfunction followed by headache and feeling unhappy or depressed. While Sierra et al,⁸ reported symptoms like difficulty in concentrating, feeling unhappy or depressed, headache and hot flushes were more prevalent, and Kapur et al,¹⁶ showed that the most prevalent symptoms were muscle and joint pains, followed by feeling tired or lack in energy, eye problems, headache and feeling unhappy or depressed. Worldwide, hot flushes are among the most commonly reported symptoms among women transitioning through menopause and in certain populations, hot flushes effect up to 75% of women undergoing this transition.^{17,18} In our study however, hot flushes and night sweats were relatively not so prevalent.

The clusters, sub-cluster and total Greene score showed an increasing trend with post-menopausal status and this findings correlates with the findings by Barentsen et al,¹⁵ where peri and post-menopausal scored significantly higher on all subscales except for depression and Sierra et al,⁸ also found higher but significant values among post-menopausal females in psychological, anxiety, somatic and total cluster.

The risk factor for the severity of menopausal symptoms among different clusters from among demographic, health, lifestyle and BMI variables was also assessed. Results from the present study showed large family size, poor health status, lower age at menarche and low quality of life were associated with higher scoring for total and different cluster. In a study¹⁹ it was suggested that women with least education were bothered more by vasomotor and general somatic problems than their better educated peer. However in our study educational level did not show significant value. In the size of the family, post-menopausal subjects who had more than 6 members showed more at risk of developing the vasomotor symptoms with significant difference. In the self-perceived health status of the post-menopausal subjects, subjects with average and poor health status were more at risk of developing the psychological, anxiety, somatic and vasomotor than the subjects with good health, but in depression and total Greene Climacteric Score no result was obtained. Statistically significant difference was seen in psychological and vasomotor functions in both poor and average health status subjects. In somatic symptoms statically significant difference was seen among subjects with poor health status. Post-menopausal

subjects with age at menarche less than 14 years of age was found to be more at risk of developing vasomotor symptoms and total Greene score than those subjects whose age at menarche was more than 14 years. Similar study by Kirchengast et al²⁰ reported significant correlation between socio-economic factors, educational level, marital status, total number of children and the degree of severity of several climacteric symptoms. In a study,²¹ vasomotor symptoms were found to be common during the menopause transition and remained elevated for some years in a majority of older post-menopausal women.

Post-menopausal females who had low quality of life were seen to be more at risk for developing all the menopausal symptoms except for depression which suggested that low quality of life were associated with high prevalence of menopausal symptoms. AlDughaiter et al,²² suggested that more severe the menopausal symptoms, the higher the MRS score and the worse the quality of life. The risk factor of BMI among underweight and overweight post-menopausal females when compared with normal post-menopausal females and were found to be non-significant for all the menopausal symptoms which contradicts the finding by Moilanen et al,²³ where higher body mass index was significantly associated with higher number of psychological and vasomotor symptoms.

CONCLUSION

To conclude, climacteric symptoms were more prevalent among post-menopausal females than pre-menopausal females. Family size, self-perceived health status, age at menarche and quality of life were independent risk factors. The present study reported significant correlation between low quality of life, self-perceived health status and the degree of severity of most climacteric symptoms among Naga females. Therefore, improving the health status and quality of life will play a vital role in reducing the risk factor for the severity of menopausal symptoms and would enhance not only the health quality but also the work output.

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Opinion

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The Current State of Professional Midwives in Japan and their Traditional Virtues

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ABSTRACT

Traditionally, Japanese women endure labor pain. They are then pleased by the sense of accomplishment after a successful vaginal childbirth, a concept based on the Japanese Buddhism. Therefore, Japanese midwives place importance on the process and devote care for pregnant women throughout the experience. Professional midwives in Japan strive to monitor the childbirth process with devotion and identify any abnormality with modern scientific knowledge in the small midwifery rooms of hospitals and clinics, in cooperation with obstetricians. Recently a new midwifery category has evolved called "advanced midwife" that do not work under a physician's direct supervision, but rather practice independently and in harmony with the doctors.

KEYWORDS: Japanese childbirth style; Midwifery; Buddhism; Perseverance.

In Sugitatsu's paper on the history of Japanese obstetricians and midwives, the *Taihouritsuryou*, an old Japanese code of laws, reported the appearance of young female doctors (probably, midwives) as low-class government officials in 701.¹ They feed pregnant women, assisted in difficult childbirth, and sometimes used acupuncture needles for treatment. In 712, the *Kojiki*, Japan's oldest history book, stated that a pregnant woman had bound a band around her belly to protect her fetus when she was in her fifth month in pregnancy. This signified that she was pregnant and included a prayer for a safe childbirth. In 1178, the *Heike monogatari*, a collection of poems composed by the members of the old aristocratic society, described five to six women surrounding a pregnant woman who leaned on and clung to the mass they assisted in the childbirth. This poem's figures show a sitting birth. From 1330, several medical schools were established, and Japanese obstetricians used herbal medicines during childbirth. In the early 17th century, midwives came into being. They emphasized that pregnant women had to bear the pain of labor earnestly, for if they managed to do so, the delivery would be easy. Women delivered in a seated posture, as described above, while pulling a rope hung from a ceiling.

Childbirths in the US were also performed in the seated position around this time and they were also aided by midwives.^{2,3} However, between the late 18th and 19th centuries, the handling of childbirth was switched from the midwife to the physician in the US ahead of Japan.

The Parisian François Mauriceau, who was a leading obstetrician in the late 17th century, advocated a reclining position in bed rather than sitting on a birthing stool or chair for childbirth.⁴ This "French Position" or "Lithotomy Position" allowed the obstetrician to more easily examine the patient and fetus during childbirth and perform any necessary procedures. Its use quickly spread in Europe and North America thereafter.

In the early 19th century, the sitting birth was still the most common childbirth position in Japan, but the merits of the dorsal position had been introduced in a book available at the time. Midwives would visit the *ubu-ya*, the birth house in a town or village, and assist childbirths and bathing of newborns. However, they sometimes called in obstetricians for help with

difficult childbirths. The midwives in those times were largely older widows. Because there was a lack of obstetrical textbooks during this time period, most midwives' knowledge was based on experience, not by studying textbook content. In short, they generally worked on past experience and perception.

In 1871, with the modernization of Japan, a medical system was established and adopted by Western European countries. A license system for midwives was also started. The common style of childbirth changed from the sitting position to a lithotomy one. Many Western doctors came to Japan to teach obstetrics and midwifery in 1910, the midwife certification examination was started. Between the late 19th and early 20th centuries, the place for giving birth shifted from one's private home to the hospitals in the US, ahead of Japan. After World War II, the baby boom in Japan swelled the population, and most deliveries were performed at home with the assistance of a midwife. However, from 1950, the numbers of childbirths performed instead at a hospital or clinic began to increase with a rate of 50% in 1960 and 99% in 1976. In 1950, 90% of childbirths were assisted by a midwife, but by 1975, a paradigm shift had occurred, and 91% of childbirths were assisted by a physician. As a result, the number of midwives who worked at midwifery homes decreased, and they instead moved to work at hospitals or clinics. In those days, they worked under physicians. Together, these changes resulted in a reduction in perinatal mortality.⁵

Before World War II, childbirth was understood to be a waiting game, in the style of the Germans which almost all Japanese obstetricians and midwives studied, in Japan. After World War II, however, efforts were made to shorten the delivery time by intervention as in the US. Women's empowerment movements in recent years have increased the average age of marriage, which has subsequently increased the rate of high-risk pregnancies as well as reduced the birth rate in Japan. Before World War II, ensuring the mother's survival was the main priority. However, after World War II, the newborn's survival also became a priority. This has subsequently increased the rate of cesarean section births, a procedure that is accompanied by a number of risks, such as pleural effusion, thrombus, hemorrhage and sepsis.

JAPANESE TRADITIONAL VIRTUES

Historically, almost all Japanese have been are Buddhists and the teaching of "Zen", a tenet of Buddhism, is ingrained in Japanese hearts, as follows: "The virtue of perseverance is needed in humans."⁶ Since perseverance means accelerating in a positive direction that leads to benefits and joy, its outcome should also be filled with goodness and joy. Buddhists with perseverance have all of the virtues. In other words, the successes experienced in the process of self-practicing and performing good deeds are dependent on an individual's perseverance. Japanese culture has long focused on praising individuals for making their best effort, not on the outcome of those efforts; as virtue is included in the process, rather than the result. Western societies, by contrast,

tend to respect the ends over the means of achieving them and think rationally and systematically by applying scientific laws.^{7,8}

RECENT CHILDBIRTH STYLES IN JAPAN

Western physicians and midwives lead modern obstetrics and midwifery and develop relevant guidelines, as mentioned above. They often use epidural anesthesia to reduce the pain of labor, and Western midwives and pregnant women regard childbirth control for the process of giving birth involving anesthesia as important. However, Japanese physicians do not use anesthesia very often during childbirth, and Japanese midwives tend to almost never use it. Traditionally, Japanese women endure labor pain, and their deliveries are silent.⁹ They are then pleased by the sense of accomplishment after a successful vaginal delivery, a concept based on the Japanese "Zen" heart. Japanese women respect the process and understand that its outcome will consequently be filled with goodness and joy. Therefore, Japanese midwives place importance on the process and devote extra care for pregnant women throughout the experience. They share in the women's pain and relieve the pain with their continuous presence, a spirit which has continued in much the same form since the early 17th century. For this reason, Japanese midwives have a negative opinion of painless labor, in contrast to Western societies. Since the early 20th century, Japanese midwives have worked to protect the perineum from injury during delivery, using a hands-on method of assistance, as they are not allow to suture perineal wounds. The suture of the perineum is the work of the doctors. The Japanese midwives take pride in a spontaneous childbirth with no lacerations. In contrast, Western midwives perform episiotomies and suture the wounds themselves with much less of a hands-on approach.¹⁰

As mentioned above, the rates of high-risk childbirth and cesarean sections are increasing in Japan. As such, professional midwives in Japan now receive the best education possible in their field and are equipped with traditional Japanese spirits for treating patients, caring for pregnant women's minds and bodies with devotion. Such professional midwives are trained to manage patients using various birth position for carrying out a normal childbirth (except for the lithotomy position), and they are trained to immediately change the position as soon as any abnormality occur. They take great effort to monitor the childbirth with devotion and identify any abnormality with modern scientific knowledge in the small midwifery rooms of hospitals and clinics, in cooperation with obstetricians. The title of "advanced midwife" was established in 2015¹¹ and these women do not work under physicians, but rather independently and in harmony with the doctors.

CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest associated with this study.

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