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Dear Colleagues,

As of January 2023, **Journal of Controversies Obstetrics & Gynecology and Pediatrics (JCOGP)** was honored with an important achievement for all the hard work done by the journal's authors, editorial review board members, and editors. **JCOGP** has been published under the Medihealth Academy. We hope to keep maintaining such honor and continue to seek external recognitions for **JCGOP** by indexing it in recognized databases.

It is a great challenge to bring a new journal into the World of Obstetrics & Gynecology and Pediatrics, with the aim of publishing high quality manuscripts. The review and articles of our young colleagues will be available to you in the first issue of our journal. Your valuable contributions and mentorships are substantial in improving the quality of manuscripts both to the authors whose work has been published in this **JCOGP** volume, as well as to the authors whose papers were not published in **JCOGP**. Your scholarly efforts are very important to ensure the quality of papers published and the success of **JCOGP**.

I would like to express my endless thanks to MediHealth Academy publishing house and Prof. Aydın ÇİFCİ, MD, who contributed to the birth of this journal with endless efforts.

The last but not least my biggest thanks is to my esteemed colleague Assoc. Prof. Tuğba GÜRBÜZ, MD, who has contributed to every aspect of this journal, on behalf of the Obstetrics and Pediatrics community, I wish the continuation of this effective performance at all times with success.

As we continue to sustain **JCOGP** as authoritative journal, we greatly appreciate your support and readership.

Best Regards,

Prof. Oya GÖKMEN, MD

Honorary Editor

Journal of
Controversies in Obstetrics & Gynecology and Pediatrics

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ORIGINAL ARTICLE

REVIEW

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Controversies in Obstetrics & Gynecology and Pediatrics

Original Article

DOI: 10.51271/JCOGP-0001

The role of preoperative transvaginal ultrasound in evaluating the myometrial invasion depth in women with endometrial cancer

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ABSTRACT

Aim: The aim of our study was to compare the results of transvaginal ultrasonography (TVS) and final pathology in the determination of the depth of myometrial invasion in endometrial cancer preoperatively.

Methods: The study was conducted as prospective observational study in a tertiary center between August 2012 -July 2012 and included 29 patients between the ages of 43 and 83 with endometrial biopsy results. Patients with endometrium cancer dignosis based on endometrial biopsy results were enrolled.

Results:. Transvaginal endometrial thickness was thicker for patients with myometrial invasion greater than ½ according to final pathology results, but this result was not statistically significant. When the patients were classified according to their surgical stages, 13 patients were stage 1a, 5 patients were stage 1b, 3 patients were stage 2, 6 patients stage 3, 2 patients stage 4. Final pathology of myometrial invasion greater than ½ patients compared with patients with thinner endometrium regarding age (p=0.003), gravidity (p=0.111), parity (p=0.135), weight (p=0.764), platelets (p= 0.831), CA125 (p=0.247) respectively. The age of patients were not statistically significant in comparison with tumor stage (p= 0.80). No statistical difference was observed when final pathology and transvaginal ultrasound results regarding myometrial invasion were compared (p= 1). We found that the sensitivity of preoperative transvaginal ultrasound for evaluation of myometrial invasion which is lesser than ½ was 77.7%. When final pathology and frozen section results were compared no significant statistical difference was found. (p=0.14).

Conclusion: In our study, we compared the results of myometrial invasion in patients with pathologic and ultrasonographic findings and we found no statistically significant difference.

Keywords: Endometrial cancer, transvaginal ultrasonography, myometrial invasion

INTRODUCTION

Endometrial cancer ranks first in developed countries and second after cervical cancer worldwide among all gynecologic cancers, also fourth among all cancers after breast, lung and colorectal cancers.[1,2] According to the decision of FIGO in 1988, endometrial cancer is a cancer that requires surgical staging. The traditional approach is midline abdominal incision followed by peritoneal washing, cytology, total abdominal hysterectomy (TAH), bilateral salpingooopherectomy (BSO), and in selected high-risk cases omentectomy, pelvic and paraaortic lenfadenectomy.[3,4] The most important prognostic factors of endometrial cancer are the histologic grade, stage of disease and the depth of myometrial invasion.[4] In a study of 1566 patients, myometrial invasion was reported to be the most important prognostic factor.[5] A direct relationship between the depth of myometrial invasion and lymph node involvement has been demonstrated in other studies.[6-8] The depth of myometrial invasion is an important prognostic factor which is directly related to the risk of disease recurrence and extrauterine disease.[9] The depth of tumor invasion in to the myometrium increases the probability of extrauterine spread and recurrence as the drainage of the lymphatic system becomes easier when the depth exceeds %50.[10,11] This is the most important pathological finding that determines whether or not lymphadenectomy should be added to surgery.

Pelvic and paraaortic lymph node metastases are directly proportional to the myometrial invasion depth and histological grade of the tumor. Magnetic resonance imaging (MRI), ultrasonography (US) and computerized tomography

(CT) were used for preoperative evaluation of endometrial cancer and to determine the depth of myometrial invasion.

The aim of our study was to compare the results of transvaginal ultrasonography (TVS) and final pathology in the determination of the depth of myometrial invasion in endometrial cancer preoperatively.

METHODS

The study was conducted as prospective observational study in a tertiary center between August 2012 -July 2012 and included 29 patients between the ages of 43 and 83 with endometrial biopsy results. Patients with endometrium cancer dignosis based on endometrial biopsy results were enrolled. Before the participation to the study patients were given informed concent which was approved by the Kocaeli University Ethics Committee (Date: 24.07.2012, Decision No: 9/12 KOU KAEK 2012/75). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

Patient's demographic characteristics (age, weight, gravidity, parity, abortion, curretage history), other co-morbidities of patients, CA125, platelet values were noted. The patients diagnosed with endometrium cancer were evaluated with MedisonSonoace X8 US using transvaginal transducer the day before the operation. All examinations were performed after the patient completely emptied her bladder in the lithotomy position. After inserting the endovaginal probe into the vagina, the vaginal probe was placed into the posterior vaginal fornix and the section of the uterus in the sagittal plane was taken. The uterus and adnexal regions were completely screened.

Uterine dimensions were measured in three different planes. In the sagittal section of the uterus, the endometrial thickness was measured from the point at which the thickness was maximum, including both endometrial layers. Myometrial invasion areas of the endometrial density extending from the normal endometrial basal layer into the myometrium were evaluated as invasion and the area reaching the deepest depth from the basal layer line was measured perpendicular to the nearest uterin serosa. The distance of the endometrial basal layer at the same point to the uterine serosa was determined.

At the end of the examination, patients were grouped according to the degree of myometrium invasion as follows:

- There was no invasion in the presence of a continuous halo surrounding endometrial echoes and no endometrial echoes extending to myometrium.
- If the ratio of the accepted distance to the whole wall is over ½, it was accepted as more than ½ invasion.
- If the ratio of the accepted distance to the whole wall is below ½, less than ½ invasion was accepted.

Preoperative TVS findings and postoperative final histopathology results were compared and the importance of TVS in determining myometrial invasion in endometrial cancer was determined.

The surgical operations of patients were performed according to frozen section and the stages of patients.

Statistical Analysis

"SPSS 21.0" statistical program was used for the statistical analysis of the collected data. For descriptive statistics, numbers and percentages were given for categorical variables, and mean, standard deviation were given for numerical variables. In the analysis of quantitative data Kruskal-Wallis test was used. Wilcoxon signed-rank test was used in the inter-group comparison of parameters. The results were evaluated to be in the confidence interval of 95% and had a significance at the level of $p<0.05$.

RESULTS

Twenty nine patients with endometrial cancer diagnosis between 43 and 83 years old were included in a study. Demographic characteristics of the patients were summarized in **Table 1**. All patients were over 154 pounds. In our patients' distribution; 1 patient had hyperlipidemia, 2 patients had hypothyroidism, 2 patients had chronic obstructive pulmonary disease (COPD), 1 patient had a history of cerebrovascular disease (CVD), and 1 patient had been treated for breast cancer.

Table 1: Demographic characteristics

	Mean±std deviation
Age	60.10±9.74
Weight	86.55±8.79
Gravidity	4.48±2.23
Parity	3.44±1.76
Abortion	0.24±0.51
Curettage	0.86±1.43

std deviation: standart deviation

Table 2 shown transvaginal endometrial thickness was thicker for patients with myometrial invasion greater than ½ according to final pathology results, but this result was not statistically significant.

Table 2: Endometrial thickness values according to final pathology

	Endometrial thickness (mean±std deviation)	P
Myometrial invasion<1/2 N=18	15.00±8.16	0.052
Myometrial invasion>1/2 N=11	22.82±12.60	

std deviation: standart deviation

When the patients were classified according to their surgical stages, 13 patients were stage 1a, 5 patients were stage 1b, 3 patients were stage 2, 6 patients stage 3, 2 patients stage 4. The operations performed according to the stages of the patients are indicated in the table. TVS was performed and hysterectomy salpingoopherectomy and lymphadenectomy were performed in 11 patients with endometrial myometrial thickness more than 1/2.

Table 3 shown endometrial carcinoma histologic types and surgical FIGO stages of patients.

Table 3: Stage and histological type of patient distribution

	Surgical FIGO Stages	
Endometrial cancer histological types		**Total**
Endometrioid	Stage IA (n=13)	27 (93.1%)
	Stage IB (n=5)	
	Stage II (n=2)	
	Stage IIIA (n=3)	
	Stage IIIC (n=3)	
	Stage IV (n=1)	
Serous carcinoma	Stage IV (n=1)	2 (6.9%)
Clear cell carcinoma	Stage II (n=1)	

Final pathology of myometrial invasion greater than ½ patients compared with patients with thinner endometrium regarding age (p=0.003), gravidity (p=0.111), parity (p=0.135), weight (p=0.764), platelets (p=0.831), CA125 (p=0.247) respectively. The age of patients were not statistically significant in comparison with tumor stage (p= 0.80).

No statistical difference was observed when final pathology and transvaginal ultrasound results regarding myometrial invasion were compared (p=1). We found that the sensitivity of preoperative transvaginal ultrasound for evaluation of myometrial invasion which is lesser than ½ was 77.7%. When final pathology and frozen section results were compared no significant statistical difference was found. (p=0.14). Distribution of patients regarding myometrial invasion by transvaginal ultrasonography, frozen section results in relation with final pathology results were given in **Table 4**.

Table 4: Distribution of patients regarding myometrial invasion by transvaginal ultrasonography, frozen section results in relation with final pathology results

	Final pathology result		Total	P
	<1/2a	>1/2b		
TVc Ultrasonography				
<1/2	14	2	16	1
>1/2	4	9	13	
Frozen Section				
<1/2	18	2	20	0.14
>1/2	0	9	9	
Total	18	11	29	

a<1/2: lesser than ½ myometrial invasion b>1/2: greater than ½ myometrial invasion
c TV: Transvaginal

DISCUSSION

While CT is better in clinical staging, its sensitivity is low in detecting the depth of myometrial invasion. The accuracy of MRI was reported to be 85%.[12] TVS is cheaper and easier to use than MRI. In our study, we showed that TVS was sensitive to the depth of myometrial invasion (77.5%).

Gordon et al.[12] in a study conducted with 25 patients in preoperative period of detecting the depth of myometrial invasion, the depth of myometrial invasion with TVS 84% accurate.

Ozdemir et al.[13] compared the TVS with MRI and reported that two techniques had the same efficiency, and also suggested doing MRI if TVS does not get sufficient results. TVS, MRI and frozen section examination of the preoperative and intraoperative diagnosis of myometrial invasion for the evaluation of the difference in myometrial invasion, although there was no statistically significant difference in the evaluation of myometrial invasion with frozen section showed beter results.

In a study of 155 women with endometrial carcinoma, Savelli et al.[14] showed that intraoperative frozen section results were more reliable than preoperative TVS in the evaluation of myometrial invasion. In our study, TVS was as reliable as the results of frozen section examination when it was confirmed by the final pathology results (in order of p=1, p=0.014). Frozen section examination should be taken in to consideration in cases where TVS is not reliable and when the decision to perform lymphadenectomy is decided.

In a retrospective longitudinal study of 187 endometrial carcinomas, TVS, MRI and frozen section showed a sensitivity of 56%, 71% and 67% and a specificity of 90%, 78% and 94%, respectively.[15]

In a country wide cohort study from Sweden which is record based for the clinical assessment of depth of myometrial invasion in endometrial carsinom, TVS was the most extensive method reported, the second common method was MRI which is followed by intraoperative gross examination, and frozen section. Most sensitivite method (90%) to find MI > 50 % was frozen section whereas the sensitivity of gross examination was lower (72%). Among the preoperative methods the sensitivity of MRI (77%) was higher than TVS (66%).[16]

In our study, 13 patients in Stage 1a, 5 patients in Stage 1b, 3 patients in Stage 2, 3 patients in Stage 3a, 3 patients in 3c and 2 patients in Stage 4 were found. The pathology results of a patient with stage 4 were classified as serous and stage 2.

Similar results were found between stage 1 hysterectomy and modified radical hysterectomy in stage 1 disease.[17] In the endometrioid group, there is said to be no need for omentectomy if there was no deep myometrial invasion or grade 3 in clinical stage 1.[18,19] In our study, hysterectomy salpingooferectomy and lymphadenectomy were performed in 11 patients with endometrial myometrial thickness more than 1/2.

Results of intraoperative frozen sections and postoperative final pathology results in 2 patients who had fibroids were incompatible. Myometrial invasion in our preoperative transvaginal application revealed that the myometrial invasion was greater than 1/2 in final pathology results of these 2 patients whose frozen section examination results were found to be less than 1/2. The preoperative TVS myometrial invasion evaluations and the final pathology results of the patients who had myoma in the uterus were incompatible with each other. Therefore, the use of TVS in the preoperative evaluation of patients with myoma seems to be causing incorrect results and incomplete operation.

CONCLUSION

In our study, we compared the results of myometrial invasion in patients with pathologic and ultrasonographic findings and we found no statistically significant difference. This statistical result showed that the pathology and ultrasound data matched. If we integrate with intraoperative frozen section pathology results, we can determine the depth of myometrial invasion with the use of preoperative TVS and decide the operation which has the least morbidity but not the worst effect to survive. Accurate detection of myometrial invasion depth with TVS in patients with uterine leiomyoma was difficult and there was no correlation with the final pathology results. The experience of the TVS practitioner affects the correct detection results. Due to the small number of patients, the findings of previous studies were not statistically significant in our study. Additional prospective studies are needed with more patients. The sensitivity of TVS is similar to the literature in our study.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of Kocaeli University Ethics Committee (Date: 24.07.2012, Decision No: 9/12 KOU KAEK 2012/75).

Informed Consent: All patients signed the free and informed consent form.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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Author Contributions: All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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Bilge Doğan Taymur

I was born in Bursa in 1981, I am married and have a child. I entered medical school, which has been my dream since I was little and graduated from Gazi Medicine in 2006. I have been in the academic area for nearly 16 years since I graduated. I am a specialist in Gynecology. My special interests are Obstetri, Endocrinology. I have been editing academic journals and books for many years. I will be happy to take part in projects that I think will benefit the health community and contribute to science.

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Original Article

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Development of marital adjustment and family functioning scale: a reliability and validity study

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ABSTRACT

Aim: We aimed to develop a novel, comprehensive scale to assess family functioning and marital adjustment.

Methods: We attempted to develop the Marital Adjustment and Family Functioning Scale with randomly selected 361 married participants without dementia and mental retardation. While calculating the internal consistency coefficient and deploying the test-retest method to ensure the reliability of the scale, we resorted to the factor analysis and criterion-related validity methods to seek its validity. The Marital Adjustment Test (MAT) and the Family Assessment Device (FAD) were utilized to ensure the criterion validity of the scale.

Results: The findings revealed the internal consistency coefficient of the scale to be 0.974. Following the test-retest study with 20 participants, we calculated the correlations between two measurements with the MAFFS test to be 0.951. Finally, we calculated the correlation coefficients between the MAFFS and the FAD and the MAT to be 0.704 and 0.775, respectively.

Conclusion: The first subscale is called the "family functioning and adjustment" since the items were oriented to assess general functions and adjustment in the family. The second subscale includes the items oriented to confidence-loyalty-violence; therefore, it is called "confidence-loyalty-violence." Finally, the third subscale is referred to as "marital dysphoria" since it attempts to assess dysphoric issues within the family. Overall, the whole scale is deemed appropriate to be called the "Berksun-Söylemez-Kayacık (BSK) Marital Assessment Scale."

Keywords: Family, marriage, marital adjustment, scale

INTRODUCTION

In its broadest definition, a family can be defined as a group of people who have kinship ties, feel close to each other, and often share the same residence. Most societies consider children the ultimate reason for existence. When it comes to family, one may recall concepts such as intimacy, economy, culture, tradition, honor, and friendship. The family can be described as the oldest, most fundamental, and most rooted institution forming the basis of society. Perhaps its most apparent task is to convey all kinds of human values to new generations and to be instrumental in the reproduction and continuation of the human species.[1] Although the definition and form of the family vary by society and culture, it has always maintained its significance as a social foundation. The previous research showed that a single type or definition of family cannot be suggested; in contrast, a family prototype has emerged over time within each society's own culture.[2]

The literature offers many definitions of family. While digging into the reasons why many definitions have been proposed for family, one may realize that family has a dynamic structure, is affected by innovations and changes, can vary by the number and characteristics of its members, and is shaped by a number of political, religious, legal, moral, and cultural elements.[3] Gladding defines family as a unit that anticipates the future with confidence and hope and trusts and protects its young members, where the members are all aware of their responsibilities and have open communication, that has clear boundaries but can be flexible when needed, and that seeks solutions for all possible problems.[4] Besides, a family can be categorized as patriarchal, matriarchal, and egalitarian by dominant character, as monogamy and polygamy (polygyny, polyandry) by the number of people to marry, as patrilineal, matrilineal, and both by the kinship of spouses, as patrilocal and matrilocal by the type of residence, and as nuclear and extended in general.

A family is established through marriage in modern societies; marriage is considered a distinguishing characteristic and the very first stage of family unity. The difference between family and marriage is uttered as follows: "Family is a group or organization, and marriage is a contract for bearing and raising

children".[5] The form and conditions of marriage, legal situations (e.g., age of marriage), and cultural changes regulate the structure and process of marriage. "Marriage is an institution, a form of a legal relationship that binds a man and a woman as spouses, provides a specific status and identity to children, and is within the control, rights, and authority of the state".[6] Framo stated that spouses are deeply attached to each other in marriage and satisfy their psychological needs (e.g., love, commitment, belonging, and happiness). He also emphasized that marriage ultimately leads to a family, meets the material and spiritual needs of its members, and ensures the safety and unconditional solidarity and sympathy between its members.[7] While defining marriage, Hansen underlined the unity between spouses, the open and reliable relationship between the members, the ability to be natural and to experience personal differences, and the satisfaction of feelings related to intimacy, anger, and sexuality.[8]

In Western societies, the search for solutions to familial problems formed the focal point of the social work profession, especially in the late 19th and early 20th centuries.[9] It is often accepted that family counseling started with Alfred Adler. Adler attached importance to preventive measures regarding mental health and attributed importance to parent education in this regard, leading him to establish family education centers in the 1920s. These centers enlightened parents and teachers about child education. Adler took a family member with a problem to meet with other family members in a family center and interviewed spouses as a couple. Moreover, he focused on interpersonal interaction based on the assumption that a disorder in a family member might not have arisen if they had lived alone.[10] "Married couples study groups" or "married couples group therapy" aimed at solving the problems between married couples, thus increasing happiness and satisfaction in marriage, initiated the born of marriage counseling, while "family education centers" can be considered the beginning of family counseling.[11] In Turkey, one may not be able to reach scholarly papers examining "family" in the pre-Republican period. The research until the 1960s often pointed out the stages of the Turkish family structure since the old Turkic communities.[12] The first empirical and large-scale studies date back to the 1960s. The changes in the 1950s also affected the family, leading family to become the subject of research in sociology. Until the 1970s, few studies focused on village and slum families. (e.g., Yasa's book titled "Ankara'da Gecekondu Aileleri" (Slum Families in Ankara) in 1960 and the studies on "Modernization Trends in Turkish Villages" by the State Planning Organization (SPO) in 1970).[13] However, the predominance of the young population, being a developing country, and the participation of women in business life led the state to focus on family studies and policies. In the 1980s and later, family studies often scrutinized "women and their problems." The review titled "Change of Family in Turkey" by the Turkish Social Sciences Association in 1984 may be shown as a noteworthy study addressing the papers on the subject. Following this period, the place of women in the family was brought to the agenda, leading the roles and statuses in the family to be questioned. The lifestyle and familial position of the woman, undertaking socialization as a wife and mother, were addressed with the changes. In the following years, the literature enjoyed increased sociological research, and the subject of the family began to be covered in doctoral and graduate studies.[14] For example, Volkan and Çevik introduced their study titled "Turkish Fathers and Families" in 1989.[15]

Measurement instruments designed for clinical settings bring practical benefits to professionals working on family and marital problems. They are particularly important to reveal possible intervention areas, provide objectivity in follow-ups, and save time. The importance of using scales in marriage and family counseling or developing novel instruments is highly acknowledged to obtain empirical information about relationships, to demonstrate problem areas to spouses efficiently, and to reveal what is needed to settle their problems.[16] The national literature seems to be dominated by adaptations of internationally-recognized instruments. For example, Çelik adapted the "Marital Satisfaction Scale" in 2006.[17] Yet, Berksun attempted to develop a scale to measure the "level of expressed emotions in families," which is thought to have an impact on the etiopathogenesis and prognosis of schizophrenia and to be a family-led factor. A total of 46 subjects, 27 of whom were relatives of schizophrenic individuals, were included in that scale development study.[18]

According to Ogburn, family functions are to satisfy economic needs, provide status, plan the education of children, provide religious education, organize leisure activities, protect family members, and create an environment of mutual affection.[19] Ackerman classified these functions as biological, social, psychological, and economic functions.[20] Epstein and Bishop perceived a healthy family as one consisting of members who can solve their problems by coming together, are emotionally connected to each other, are concerned in a way of not preventing their freedom, can effectively fulfill their roles, can control each other's behavior, and have an open, relaxed, and direct communication between them.[21] In this regard, Yörükoğlu stated, "People from healthy families are often mentally healthier, exhibit less depression and skepticism, and do not immediately worry about adverse events. They can relate better with those around them and think positively about the future. On the other hand, those coming from dysfunctional families show introversion, dependency, and skepticism, are unable to establish good relations with others, and have a negative view of the future.[22] Emphasizing the importance of communication and cooperation, Pollak argued that the interaction patterns in healthy marital relations should be based on the assumption of mutual satisfaction and that some problems depending on age and marriage can be eliminated thanks to positive communication and cooperation in healthy families.[23] Ackerman highlighted that couples in a healthy family have congruence in their marital roles, share common goals and values, and cooperate in seeking appropriate solutions regardless of the extent of the problems. Continuing a comprehensive description of a healthy family, he also stated that such couples do not have feelings of guilt, do not show behaviors such as overly dumping a member or making them a scapegoat, accept each other as they are, respect each other and understand the changes, and, most importantly, utilize all these behaviors as a means to improve their relationship.[24] One can think of the opposite of the above-mentioned qualities when it comes to an unhealthy family. Families are often considered unhealthy when the members avoid communication, seek solutions on issues concerning the family, do not/cannot establish true intimacy with each other, and have negative feelings.[25] It is clearly an undesirable environment where the family members are deprived of communication and interaction, cannot cope with any crises,

end up with insolvency in problems, are always in constant conflicts, adopt diverse ego ideals, do not have flexibility, and experience chaos. The burden of stress in this unhealthy environment on the members and dysfunctional solutions for this situation (e.g., turnover of those assuming a role in the family, changes to the roles, or having to assume an irrelevant role in the family) can lead to a vicious circle of such an unhealthy environment.[26]

It is not prudent to show a moment without communication in the family since it is a dynamic structure. Therefore, it can confidently be asserted that family communication is one of the factors affecting happiness in marriage. Griffin and Greene grouped intra-familial communication into verbal/non-verbal communication and spousal communication/spouses' communication with other family members.[27] Fowers, on the other hand, mentioned two fundamental tasks of intra-family communication. The first is to bring affective intimacy where spouses exert efforts to mutually understand each other, while the second is to help settle life difficulties creating communication barriers.[28] Family problems are often caused by a lack of or disruptions of communication. Communication problems in the family may cause the following: a) each family member's thinking only of themselves, b) negative approaches and no respect for each other's feelings, needs, and desires, c) no support for each other, d) hindering each other's freedom by putting definite values and behaviors, e) lack of experience of positive and meaningful relationships, f) lack of communication between family members, and g) misunderstanding of each other.[29]

The scholarly interest yielded some theories/approaches to better understand the concepts of family and marriage: systems approach, structural approach, behavioral approach, communication approach, cognitive approach, strategic approach, psychoanalytic/psychodynamic approach, experiential approach, and developmental approach.

METHODS

This study was produced from the author's specialization thesis numbered 14-287 and titled "Development of marital adjustment and family functions scale: a reliability and validity study." The study was carried out with the permission of Ankara University Faculty of Medicine Ethics Committee (Date: 07.19.2010 Decision No: 14-287). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

This is a scale development study covering item pooling and selection and seeking validity and reliability. While the population consisted of the author's social milieu and the patients hospitalized in the psychiatry ward of the Ankara University Faculty of Medicine, the sample included randomly selected 361 married participants without dementia or mental retardation. Among them were also ten hospitalized participants, four of whom were diagnosed with depression, three with anxiety disorders, and three with somatization disorders.

Three academics, who are well-versed in the subject, generated a pool of 600 items considering both the conceptual frameworks in the relevant literature on the family and the previously developed instruments. The preliminary draft included 248 items after 352 were eliminated for various reasons (overlapping, ambiguity, etc.). This draft was first submitted to 118 subjects on a 3-point Likert-type scale ranging from 0 (disagree) to 2 (agree). Then, the second draft included only those with an item-total correlation coefficient above 0.20. The second draft was then submitted to 500 married couples in a pilot study. We performed a factor analysis on the data from 264 valid responses and finalized the scale with 99 items.

Statistical Analysis

We performed the statistical analyses on the SPSS 17.0 program. Initially, responses were scored from 2 (agree) to 0 (disagree), and the positive items were reversely coded.

RESULTS

The findings revealed the mean age to be 36 years (21-65 years) and the mean length of education to be 13 years and (5-17 years). Moreover, the mean length of marriage was found to be 11 years (1-48 years). There were almost the same numbers of females (52%) and males (48%) in the study, and no participants had more than two marriages. Almost all the participants (98%) were married once, and most of the participants (90%) hosted no person at home other than their spouses and children. A quarter of the participants had no children, 33% had an only child, 31% had two children, and 8% had three children. **Table 1** presents the participants' demographic characteristics.

Table 1. Participants' demographic characteristics

	Age	Length of education	Number of marriage	Length of marriage	Additional person at home	Number of children
N						
Valid	345	345	346	346	346	346
Missing	16	16	15	15	15	15
M	36.2841	13.8580	1.0231	11.1618	.1387	1.2977
SE	.50673	.13738	.00809	.54571	.02545	.05570
SD	9.41210	2.55181	.15051	10.15088	.47347	1.03607
Variance	88.588	6.512	.023	103.040	.224	1.073
Range	44.00	12.00	1.00	47.00	4.00	6.00
Min.	21.00	5.00	1.00	1.00	.00	.00
Max.	65.00	17.00	2.00	48.00	4.00	6.00
Percentiles						
25	29.0000	11.0000	1.0000	3.0000	.0000	.0000
50	33.0000	15.0000	1.0000	7.5000	.0000	1.0000
75	42.0000	15.0000	1.0000	17.0000	.0000	2.0000

The reliability of the 99-item MAFFS was sought by calculating its internal consistency coefficient and using the test-retest method. Accordingly, we calculated the internal consistency coefficient of the scale to be 0.974. In the test-retest phase, we readministered the scale to 20 participants and found a perfect correlation between the measurements (r = 0.951). When it comes to criterion validity, we considered the correlations between the MAFFS score and the scores on the FAD, MAT. Accordingly, the correlation coefficients between our scale and FAD and MAT were found to be 0.704 and 0.775, respectively. The results are presented in **Table 2**.

Table 2. Criterion-related validity of the MAFFS with the FAD, the MAT, and the BDI

Correlations	BDI	MAFFS	FAD	MAT
BDI				
Pearson Correlation	1	.548**	.519**	-.561**
Sig. (2-tailed)		.000	.000	.000
N	276	217	220	205
MAFFS				
Pearson Correlation	.548**	1	.704**	-.775**
Sig. (2-tailed)	.000		.000	.000
N	217	264	209	193
FAD				
Pearson Correlation	.519**	.704**	1	-.728**
Sig. (2-tailed)	.000	.000		.000
N	220	209	271	197
MAT				
Pearson Correlation	-.561**	-.775**	-.728**	1
Sig. (2-tailed)	.000	.000	.000	
N	205	193	197	244

DISCUSSION

The Marital Adjustment Test (MAT), developed by Locke and Wallace in 1959, consists of 15 items.[30] The original study sought the reliability and validity of the instrument with 118 men and 118 women not married to each other. For further validity, the authors compared the scores of 22 men and 26 women who were divorced, living apart, or undergoing marital therapy and the scores of 48 couples perceived as congruent by their relatives. It was observed that the scale significantly differentiated the compatible and incompatible groups. The clinical interviews yielded that only 17% of the group perceived as incongruent and 96% of the group defined as congruent got a score of 100 or higher, indicating good marital adjustment. The MAT was adapted into Turkish by Tutarel Kışlak.[31] The author sought criterion-related validity of the MAT using the Interpersonal Relationship Scale (IRS) and the Attribution Questionnaire (AQ). Accordingly, the correlation coefficients between the total scores were found to be 0.12 and -0.54, respectively. On the other hand, in the construct validity of the adapted scale, the same factorial structure was obtained as in the original study. The author considered internal consistency, split half-test reliability, test-retest reliability, and item test correlations for reliability concerns of the MAT. Accordingly, she found the internal consistency coefficient to be 0.84, the split half-test reliability coefficient to be .84, and the test-retest reliability coefficient to be 0.57.

The 60-item Family Assessment Device (FAD) measures family functions within six dimensions. The battery that can be administered to all family members over 12 years consists of seven subscales: problem-solving, communication, roles, affective responsiveness, affective involvement, behavior control, and general functioning. A high score on the scale indicates impaired functioning. The family score can be obtained from the mean scores of all family members. Epstein mentioned the psychometric properties of the FAD and reported sufficient internal consistency (0.72-0.92) and test-retest reliability (0.66-0.76) of the subscales, a moderate relationship with other family functioning scales, and low correlation with social desirability.[32] Clinicians previously discovered that each subscale of the FAD distinguished families as healthy and unhealthy. The FAD was adapted into Turkish by Bulut.[33] The author sought its reliability by adopting internal consistency reliability and score invariance and calculated Cronbach's alpha coefficients for the subscales to be between 0.38 and 0.86. Moreover, test-retest correlation coefficients of the subscales were found to be between 0.62 and 0.90. Furthermore, the construct validity of the adapted FAD was sought with the groups with and without psychiatric patients who were in the process of divorce and not. The results showed that the adapted scale significantly distinguished the groups. Finally, the criterion-related validity of the instrument scale was explored using the Married Life Scale (MLS) on 25 married couples. The correlation between the general functioning subscale and the MLS was calculated to be .66. Overall, these findings yielded sufficient psychometric properties of the Turkish version of the FAD.[33]

We subjected the final draft of the 99-item MAFFS to a three-way factor analysis and found no change in its factorial structure and factor loadings of the items. It was also observed that there were enough differences between the factor loadings of the items to be reclustered under other factors.

The items in the first subscale (42 items; sample items: "I think my spouse is/will be a good parent" (item 18), "I usually feel close to my spouse" (item 11), "I mostly enjoy spending time with my spouse" (item 13), "Our arguments and struggles usually result in reconciliation" (item 15), "My spouse appreciates and likes me" (item 21), "My spouse often knows how to apologize when behaving wrong" (item 19), "I think we have a congruent relationship" (item 166), "We chat while eating" (item 14), and "We make decisions about our family together" (item 70)) are all related to the general functioning and marital congruence in the family. Thus, it was deemed appropriate to call this subscale "family functioning and adjustment."

The second subscale (30 items; sample items: "I think my spouse is prone to extramarital affairs" (item 175), "I have experienced physical violence from my spouse in the last year" (item 137), "I think my spouse shares martial issues with everyone except me" (item 160), "I think my spouse is a liar" (item 181), "My spouse brings up divorce following every argument" (item 143), "My spouse often uses verbal and emotional violence against me" (item 133), "My spouse thinks that I will be unfaithful to her/him; s/he does not trust me" (item 132), "I think my spouse is prone to physical violence" (item 85)) was discovered to assess trust, loyalty, and violence within the family. Thus, we thought that it could represent the construct of "trust-loyalty-violence."

The items on the third subscale were thought to be related to "marital dysphoria" as they reflect the hostile emotional atmosphere with dissatisfaction, distress, sadness, blame, or accusation between spouses; therefore, it was called "marital dysphoria." (sample items: "My spouse sees me as a biased person" (item 146), "I think that I mostly overwhelm my spouse" (item 158), "I often think that my spouse does not understand what I feel and go through" (item 189), "I think that my spouse is more fond of her/his mother/father/siblings (her/his own family" (item112), "My spouse makes me feel guilty about many issues" (item 126), "My spouse thinks I am a rather demanding person" (item 126), "My spouse makes me feel guilty about many issues" (item 135), "I increase the frequency of my suggestive speech and behaviors when thinking that my spouse does not understand me" (item 198), "I think my spouse criticizes me too much" (item 199), and "My spouse always thinks that I am indifferent to her/him" (item168).

A measurement tool must be reliable and valid to be utilized in clinical practice. In this study, while we tested the reliability of the MAFFS based on internal consistency reliability and test-retest methods, its validity was sought based on construct validity and criterion-related validity. Prior to the validity and reliability study, we attempted to reduce the number of items on the 208-item draft MAFFS. Accordingly, we intentionally included the same or similar items, which were predicted to positively or negatively affect the internal consistency of the scale if responded differently, in the draft form. As a result of evaluating these items in two stages by their internal consistency/test-retest/item-total coefficients and factor loadings, they were found to be responded in a way that would not disturb the consistency of the test structure. After eliminating these items, we applied reliability and validity tests for the 99-item final draft.

In the reliability phase, the number of participants validly responding to the scale items became 264 since 97 participants left missing items on the scale. However, we discovered that the missing items were not related to a specific domain (e.g., sexuality). Then, we calculated Cronbach's alpha coefficient of the scale and obtained almost perfect internal consistency (0.974) of the scale for 264 subjects. It is expected for the internal consistency coefficient to appear low as the number of items decreases. Nevertheless, we did not experience a dramatic reduction in the internal consistency from the 208-item draft form (0.986) to the 99-item final form (0.974), suggesting that the MAFFS demonstrates a robust internal consistency and factorial structure. In the test-retest measurements, we calculated the correlation coefficient between the test-retest MAFFS scores to be 0.951. It was caulked to be 0.875 for the family functioning and adjustment subscale, 0.785 for the trust/loyalty/violence subscale, and 0.696 for the marital dysphoria subscale. Therefore, the test-retest reliability of the MASS tested with 20 participants at three-week intervals documented the temporal reliability of the scale.

We sought the construct validity of the MAFFS on three-way factorial analysis based on the varimax rotation method. Accordingly, we concluded that the factorial structure of the scale was preserved after removing similar/same items with less distinctiveness. On the other hand, we used the FAD and the MAT to seek the criterion-related validity of the scale. The results showed good correlations between the MAFFS and the FAD (0.704) and the MAT (-0.775), indicating that the MAFFS yielded sufficient validity to be utilized.

CONCLUSION

Overall, the MAFFS can confidently be utilized in research with further evidence by future studies since it was developed from scratch relying on our society/culture and showed good correlations with similar instruments introduced before..

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of Ankara University Faculty of Medicine Ethics Committee (Date: 07.19.2010, Decision No: 14-287).

Informed Consent: All patients signed the free and informed consent form.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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Maternal serum 25-hydroxy vitamin D level in first-trimester pregnancy loss

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ABSTRACT

Aim: Pregnancy loss (abortus) is defined as loss of fetal cardiac beat or expulsion of pregnancy material before 20 weeks. It has many causes such as chromosomal abnormalities, uterine anomalies, infections, and unknown causes. Vitamin D has become one of the new topics of research in many medical fields, as it has relations with other diseases besides bone diseases. In some studies of recurrent pregnancy loss, a low vitamin D level was found. In our study, vitamin D levels were measured in the first-trimester pregnancy loss and normal pregnancy group.

Methods: Patients, single pregnancies with a positive fetal heartbeat, who applied to the pregnant outpatient clinic for the first examination of pregnancy were included in the study, and vitamin D levels were measured at this time. The patients were followed up to the 12th gestational week using the hospital automation system. The groups of normal pregnancy and abortus groups were determined. 25-hydroxy (25-OH) vitamin D levels between 2-96 ng/ml can be detected, while over 30 ng/ml is sufficient, 20-29.99 ng/ml is insufficient, and <20 ng/ml is defined as a low 25(OH)D3 level.

Results: 66 patients were included in the pregnancy loss group, in the follow-up, 63 patients were in the normal pregnancy group. The mean vitamin D level of the individuals included in the study was measured as 7.45±4.64 ng/ml. Levels of vitamin D were 10.04±6.19 in the normal course group and 4.8±1.73 ng/ml in the intrauterine exitus group ($p<0.05$). At a vitamin D level of 6,87 ng/ml, pregnancy loss was expected with 90% sensitivity and 64% specificity.

Conclusion: It is still an important issue to determine the most appropriate level and preconceptional starting and the appropriate dose for maximum benefit for mother and baby, especially in the reproductive period and pregnant. Therefore, large-scale randomized controlled studies of high quality are needed.

Keywords: Abortus, 25-Hydroxyvitamine D3, pregnancy loss

INTRODUCTION

Spontaneous abortus is described as fetal loss before 20 gestational weeks. Definition of abortus by the World Health Organization (WHO) is; loss of a fetus or embryo that weighs less than 500 grams. While spontaneous abortus is the most seen complication of early pregnancy, its incidence decreases as an increases in the gestational week of pregnancy.[1] Incidence is approximately 8-20% of pregnancies.[2]

The risk factors best associated with pregnancy loss are advanced maternal age, history of abortion, and maternal smoking. Smoking large amounts (more than 10 cigarettes per day) increases the risk of pregnancy loss.[3] Alcohol, cocaine, and nonsteroidal anti-inflammatory drug usage is also a risk factor for abortus. Pre-pregnancy body mass index (BMI) below 18.5 or above 25 kg/m2 was associated with infertility and spontaneous abortion.[4] Chromosomal anomalies are found in 50% of the abortus material. While there is an abnormal fetal karyotype in 90% of pregnancies with an empty sac, this rate is 50% at 8-11 weeks and 30% between 16-19 weeks.[1]

Although these reasons are found, this issue is still not fully resolved. Until a few years, 25-hydroxy (25-OH) vitamin D was seen as the 'bone vitamine', but recently it has been found to affect cancer, metabolic syndrome, infections, metabolic and neurological diseases, even pain. In addition, associations with low vitamin D levels and preeclampsia, gestational diabetes mellitus, hyperemezis gravidarum and preterm birth are found.[5,6]

METHODS

This study was produced from the first author's specialization thesis in gynecology and obstetrics numbered as 10507811 and titled "Maternal serum 25-hydroxy vitamin D

level in first-trimester pregnancy loss". It is aimed to compare vitamin D levels in first-trimester pregnancy loss with those of individuals who did not experience pregnancy loss.

Approval for this thesis study was obtained from Ankara Dr. Zekai Tahir Burak Women's Health Training and Research Hospital Education Planning and Coordination Department (Date 24.01.2014, Decision No. 22). This study had been performed in accordance with the ethical standards described in an appropriate version of the 1975 Declaration of Helsinki, as revised in 2013.

Patients, single pregnancies with the positive fetal heartbeat, who applied to the pregnant outpatient clinic for the first examination of pregnancy were included in the study. Patients under the age of 18 and over 35 years of age, those with a history of recurrent abortion, pregnancies using assisted reproductive techniques, thyroid disorders, a history of thrombophilia, diabetes mellitus, patients with antiphospholipid syndrome, and those using vitamin D supplements were not included in the study.

All participating pregnant women were informed about the study and obtained informed verbal consent. Pelvic and physical examinations of all cases were performed, and age, obstetric history, and family history were recorded. In addition, the weight and height of the patients were measured and recorded. The gestational week was calculated to the last menstrual period and biometric measurements made with Toshiba Aplio 500 7.5 Mhz vaginal probe for ultrasonography were calculated. From the patients with a positive fetal heartbeat and who met the study criteria, 2 ml of morning fasting blood sample was taken into an EDTA-free biochemistry tube with a vacutainer from the antecubital vein under sterile conditions centrifuged at 4000 rpm for 10 minutes. The serum samples were stored at -80°C in the Biochemistry Laboratory until the study. stored in the refrigerator.

The patients were followed up to the 12th gestational week using the hospital automation system. The group without pelvic pain and vaginal bleeding until the 12th gestational week was defined as the normal healthy group. Pregnancy loss was defined as patients whose fetal heart rate was negative before the 12th week or whose pregnancy material was completely or partially discarded due to vaginal bleeding.

25(OH)D3 levels in blood samples of selected patients were studied on Elecsys 2010 autoanalyzer (Roche Diagnostics, Mannheim, Germany) by electrochemiluminescent immunoassay (ECLIA) method using original reagents (05894913, Roche Diagnostics, Mannheim, Germany). Results were calculated as ng/ml. (1 ng/mL is equivalent to 2.496 nmol/L.) With this method, 25(OH)D3 levels between 2-96 ng/ml can be detected, while over 30 ng/ml is sufficient, 20-29.99 ng/ml is insufficient, and <20 ng/ml is defined as a low 25(OH)D3 level.

Statistical Analysis

IBM SPSS Statistics 16.0 (IBM Corp. Released 2007. IBM SPSS Statistics for Windows, Version 16.0. Armonk, NY: IBM Corp.) program was used for statistical analysis and calculations. Statistical significance level was accepted as $p<0.05$. The conformity of the continuous variables in the study to the normal distribution was evaluated with the Kolmogorov-Smirnov test. In addition, number (n) and percentage values were given for categorical variables such as the result of pregnancy follow-up, and smoking status obtained within the scope of the study.

Differences between groups according to the course of pregnancy in terms of age, BMI, and gravida were evaluated by an independent t-test. In addition, vitamin D levels were categorized and the relationship between the groups was evaluated with the chi-square test. Finally, the appropriate cut-off value was determined by finding the sensitivity and specificity values for the outcome of pregnancy loss for the vitamin D level.

RESULTS

A total of 472 patients with positive fetal heartbeat at the first pregnancy examination and meeting the study criteria were included in the study. Pregnancy results of 15 patients could not be reached in the follow-up. While 66 patients were included in the pregnancy loss group in the follow-up, 330 patients remained in the pregnancy group with a normal course. 63 patients were selected from the normal pregnancy group by randomization according to the demographic characteristics of the other group.

The mean vitamin D level of the individuals included in the study was measured as 7.45±4.64 ng/ml. Levels of vitamin D were 10.04±6.19 in the normal ongoing group and 4.8±1.73 ng/ml in the intrauterine exitus group($p<0.05$).

When individuals were separated according to age, weight, and body mass index, no significant difference was found between vitamin D levels ($p>0.05$).

Vitamin D levels were classified as levels according to the kit studied; when <20 ng/ml low, 20-29.99 ng/ml deficient levels and >30 ng/ml levels are considered normal and vitamin D levels are recategorized,

Since the number of individuals in some compartments was less than 5 in the evaluation, the vitamin D levels were reclassified as <20 ng/ml and 20 ng/ml and above and reevaluated according to the pregnancy follow-up results;

There was no significant relationship between these vitamin D levels and pregnancy outcomes($p>0.05$). In Table 3; the cut-off value for vitamin D was mentioned for the pregnancy loss group. At a vitamin D level of 6,87 ng/ml, pregnancy loss was expected with 90% sensitivity and 64% specificity.

Table 1. Descriptive values of study groups

Study groups	Healthy group n=63		Pregnancy loss group (n=66)		P
Variables	Mean	Min-max	Mean	Min-Max	
Age (year)	26.58±4.01	19-34	24.12±3.89	18-33	NS
Gravidity	1.57±0.75	1-3	1.41±0.7	1-5	NS
Body mass index (kg/m^2)	25.09±3.42	18-33	24.96±4.46	19-42	NS
Smoking status	61 non-smoker	2 smoker	62 Non-smoker	4 smoker	NS
Full covered Clothing	22 full-covered	41	21 full-covered	45	NS

NS: not statistically significant($p\geq0.05$)

Table 2. The relationship between the outcome of pregnancy follow-up and vitamin D levels

Level of vitamin D (ng/ml)	Number of patients N	
	Normal	Intrauterine exitus
Low (<20)	56	57
Deficiency(20-29.99)	5	8
Sufficient(>30)	2	1

Table 3. Cut-off values of vitamin D levels in pregnancy loss group

Cut-Off	Sensitivity	Spesificity
6,78	0,892	0,644
6,87	0,908	0,644
6,96	0,908	0,630

DISCUSSION

Vitamin D has become one of the new topics of research in many medical fields, as it has relations with other diseases besides bone diseases.

Although the levels of vitamin D in women vary, in the first trimester, Korean women's median vitamin D level is 9.22 ng/ml, which is probably related to low vitamin D intake.[7] On the other hand, the serum 25(OH)D3 level in all women between 13-44 in the USA was 23 ng/ml (95% confidence interval; 22-24).

Serum 25(OH)D3 levels were higher in pregnant women than nonpregnant women. In our study, the average level of vitamin D was 7.45 ng/ml, and 85.6% of the pregnant women had a vitamin D level below 20 ng/ml and it was found to be at the insufficiency level.

As in other studies, no difference was found between vitamin D levels according to age. In one study, young age, low socioeconomic status, pregnancy, and not using late trimester vitamin D supplements were also found to be independent factors. In our study, the first trimester values were examined, and those who used any vitamin D supplements were not included in the study. Therefore, we think that the low vitamin D levels in our study are due to both insufficient intake and not using any supplements.

Although sunlight is the strongest source of vitamin D in summer, the importance of special supplements or fortified foods increases in northern latitudes (40°N). It is included in diet recommendations in most European countries, America, and the world.[8,9] It should be taken at a daily dose of 1,800-4,000 IU to maintain the 25(OH)D3 level at 75-110 nmol/l and to see optimal benefits.[10] Supra physiological toxic levels are above 150 nmol/L. In our study, the rate of pregnant women with optimal vitamin D levels (≥20 ng/ml /50 nmol/L) was 14.4%.

Vitamin D is thought to have immunomodulatory and anti-inflammatory effects by regulating the production and function of neutrophil degranulation products and cytokines. Various cells in the immune system have vitamin D receptors and are modified with vitamin D.[11] Although vitamin D is responsible for suppressing the acquired immune system, it also increases the innate immune response. In addition, it reduces the production of inflammatory cytokines such as IL-1,6, and TNF in cellular immunity.

Active 1.25(OH)D3 is synthesized in human decidual cells. Therefore, most studies show that vitamin D is acquired in fetal-maternal encounters during gestation and is involved in the innate immune response.[12-14] In addition, myometrial contractility is also dependent on calcium release, which is regulated by vitamin D.

The human placenta synthesizes everything needed for vitamin D signals, such as VDR, RXR, CYP27B1, and CYP24A1. Weisman et al.[15] found that human placental and decidual tissues synthesize 1.25(OH)D3 and 24.25(OH) D3. Supporting these findings, cultured human primary syncytiotrophoblasts and decidual cells produce 1,25(OH) D3 and secrete the active form into the culture medium. With an increased amount of 1,25(OH)D3, the transcription of CYP27B1 is decreased in human cytotrophoblasts and syncytiotrophoblasts, while transcription of CYP24A1 is increased.[16] VDR antagonists reduce 1,25(OH)D3-induced CYP24A1 levels.

Insulin-like growth factor (IGF-1) is a key regulator of fetal growth and hydroxylation of 25(OH)D3 in cultured placental cells.[17] 1,25(OH)D3 granulocyte-macrophage colony-stimulating factor 2 (GMCSF-2) increases cAMP while inhibiting TNF-a, IL-6.

A decrease in infection rates and cell death were found with vitamin D treatment, possibly due to increased cAMP levels.[14] This finding supports that vitamin D supplementation reduces infection during pregnancy. Although the effect of infection in recurrent abortions has not been proven, the infection mechanism may be effective in abortion.

Vitamin D and calcium metabolism change during pregnancy. Calcium passes from the mother to the fetus through the placenta. In rats, the placenta passes 25(OH) D3 and 24.25(OH)D3 but not 1.25(OH)D3.[18] Although transplacental transport has not been studied in humans, the maternal-to-fetal transmission of vitamin D is facilitated by the greater availability of 1,25(OH)D3 in the maternal circulation than in the fetus.[19] The synthesis of 1,25(OH)3D increases in the kidney during pregnancy. However, vitamin D levels in pregnant women were insufficient in our study. Transplacental transmission in humans has not been studied, and fetal levels in pregnant women who already have insufficient amounts of vitamin D are also controversial.

Optimal serum levels and the required amount for pregnancy are unknown.[9,20] Although doses of 400, 800, and 1,600 IU are small and have little effect on vitamin D levels in pregnant women, in a recent randomized controlled trial.[21] Vitamin D initiated at a dose of 4,000 IU/day per week was found to be safe and achieved adequate levels in the mother and newborn regardless of race.[22] Although those who used vitamin supplements were not included in our study, there are doses of 500IU in our country's preparations recommended for pregnancy. It is controversial how adequate this dose is for pregnant women.

Although the trans-placental transmission of vitamin D in humans is unknown, local vitamin D synthesis in the human placenta and decidua, the presence of hydroxylation enzymes, and the presence of the vitamin D receptor have

revealed the importance of this hormone in reproductive function.[23] Recent studies supported this by the detection of the vitamin D receptor in the rat endometrium in the oestrus cycle. Although it is prominent for its local effect, many studies have been carried out in the fetomaternal field because it is a powerful immunoregulatory molecule in various studies.

1,25(OH)2D3 inhibits IL-12 and increases the release of IL-10 in dendritic cells. The cytokine profile shifts to the TH2 phenotype.[24] The possible vitamin D mechanism is locally effective. To demonstrate this, tissue and enzyme studies are needed by taking samples from the endometrium. In this regard, Thota et al.[25] uterine smooth muscle cells are cultured in an inflammatory environment, in culture with monocytes, when vitamin D treatment is given, IL-1b, -6,-13, TNFα, connexin-43, prostaglandin receptor, oxytocin, estrogen receptor a, progesterone receptor A/ In the B ratio, a decrease in the nuclear fraction of p-IkBa and NFkB-p65 in the cytosol was detected. These results show that vitamin D reduces inflammation and inflammation-induced markers and contraction-related factors in uterine smooth muscle via the NFkB pathway. Furthermore, D vitamin D treatment reduces cytokines' synthesis in decidual natural killer cells and reduces inflammation triggered by infection.[26]

A low progesterone A/B ratio means high affinity for progesterone and is responsible for maintaining uterine silence.[27] Thota et al.[25] defined that progesterone receptor A/B ratio decreased with vitamin D treatment. It has been observed that vitamin D also reduces NFkB activity in macrophages, thus inhibiting NFkB-activated inflammation and providing myometrial silence during gestation. These mechanisms explain the effect of vitamin D on both abortion imminens and pregnancy loss. Local mechanisms provide the effect.

The study measured vitamin D levels with the ELISA, RIA, EIA methods on the market or the gold standard HPLC method. When these methods were compared, it was determined that HPLC/mass spectrometry was better than colorimetric methods and there were measurement differences between other methods.

In our study, the sensitivity for the cut-off point of 6.87 ng/ml was 0.908 and the specificity was 0.644. Therefore, the area under the curve is 0.817, may be considered a good test. Sensitivity and specificity values for other cut-off points that can be used should also be reconstructed according to the reference values in the table according to the populations. Cut-off values should be determined according to pregnant women, trimester, and population. The results of our study may depend on the method used and may need to be confirmed by the gold standard HPLC/mass spectrometry.

Normal levels of vitamin D were twice as high in white women as in black women (50-60 mmol/L vs. 20-30 mmol/L, respectively). Absorption through the skin is the main source of vitamin D and UV-B rays are necessary to initiate the cascade. Although melanin is more common in dark skin, absorption is reduced in very dark skins as it does not pass UV-B.[28] In our study, vitamin D levels were similar in general, which may be because the population is from the same race.

Low vitamin D levels can be caused by limiting skin exposure due to cultural and religious beliefs. For example, in the study of Holmes VA et al.[29] veiled women in the Victorian region of Australia, although sunlight is sufficient in Australia, 91% of women had a vitamin D level below 9 ng/ml. In our study, no difference was found between the groups according to the veiling status of pregnant women.

Today, the efficacy and safety of vitamin D supplementation are limited. In addition, most studies have been conducted in different ethnic groups, with inconsistent results.

There is insufficient evidence to suggest that low vitamin D levels in early pregnancy are associated with poor pregnancy outcomes. However, our study found a relationship between early pregnancy loss and vitamin D deficiency, and the results may be due to different populations.

Chromosomal anomalies are involved in the etiology of abortion at a rate of 50%, and this rate is 41% in abortions without fetal heartbeat detected in early pregnancy loss. Our study excluded the etiology of the chromosomal anomaly since pregnancies with positive fetal heartbeat at the beginning were included. However, there is no clear result since karyotype is not checked from the abortion materials. Abortions due to maternal reasons such as uncontrolled glycemic, diabetes mellitus, Cushing's syndrome, PCOS were excluded since these patients were not included in the study. Although possible uterine anomalies such as uterine septum are unknown, chemical exposures such as mercury are also unknown. The immunological effect is considered in the unexplained group in the etiology of abortion, and the vitamin D mechanism may be acting through this possible pathway.

CONCLUSION

Vitamin D deficiency is still a long-standing problem for healthcare professionals and the public. Newborns, children, pregnant, and postmenopausal women are at risk. Most human results are the results of animal and laboratory studies and do not show a cause-and-effect relationship. Well-designed clinical studies are few and available information is limited. The differences in the results of the studies are due to the methodology and genetic, ethnic, and racial differences, latitudinal and seasonal differences. Vitamin D deficiency is usually not recognized clinically, but laboratory measurements are easy and treatment is inexpensive. Oral supplementation is the best tolerated and most effective. However, the optimal level of the effect of vitamin D in the reproductive period is not clear. It is still important to determine the most appropriate level and preconceptional starting and the appropriate dose for maximum benefit for mother and baby, especially in the reproductive period and pregnant. Large-scale randomized controlled studies of high quality are needed. By confirming the experimental results of vitamin D deficiency and risks, public health practices can be started.

ETHICAL DECLARATIONS

Ethics Committee Approval: Approval for the study was obtained from Ankara Dr. Zekai Tahir Burak Women's Health Training and Research Hospital Education Planning and Coordination Department (Date: 24.01.2014, Decision No: 22).

Informed Consent: All patients signed the free and informed consent form.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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Author Contributions: All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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I was born in Trabzon in 1985, I have one child. I entered medical school, which has been my dream since I was little and graduated from Marmara University School of Medicine in English in 2010. I have been in the academic area for nearly 13 years since I graduated. I am a specialist in obstetrics and gynecology. My special interests are urogynecology and high- risk pregnancies. I have been editing academic journals and books for many years. I will be happy to take part in projects that I think will benefit the health community and contribute to science.

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Comparison of laparotomy and laparoscopy in hysterectomies for benign uterus diseases

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ABSTRACT

Aim: To compare the difference between laparoscopic (L/S) and laparotomic (L/T) hysterectomies and the addition of oophorectomy to surgery by complications, blood transfusion, and changes to hemoglobin (Hb) levels and explore the impacts of diabetes mellitus (DM), smoking, previous abdominal surgery, and body mass index (BMI) on early and late complications.

Methods: We recruited 537 patients for this retrospective cross-sectional study. The patients were initially divided into two groups: L/S and L/T and were further divided into subgroups by the addition of oophorectomy. We then compared the groups by early and late complications, changes to Hb levels, and blood transfusion. Moreover, we explored the associations between early and late complications and DM, previous abdominal surgery, and smoking.

Results: The findings revealed that 22.7% of hysterectomies were L/S, and 77.3% were L/T. We concluded similar results between main groups and subgroups. Yet, we could not reach significant impacts of BMI, DM, smoking, and abdominal surgery on complications. Even though postoperative blood transfusion was found to be significantly higher in the L/T group than L/S group (L/S: 0.8%, L/T: 5.8%, p=0.022), it did not significantly differ between the subgroups (Group 1: 3.3%, Group 2: 0%, Group 3: 6.5%, Group 4: 5.5%, p= 0.114). Besides, 6.7% of the patients developed complications. We discovered surgical site infection in 3% of the patients, bleeding and hematoma in 1.6%, and urinary tract injury in 0.9%, while there was only one mortality.

Conclusion: Overall, we could not conclude a significant difference between L/S and L/T hysterectomies for benign reasons, except by postoperative blood transfusion. Moreover, oophorectomy did not contribute to the risk of surgery-related complications and blood transfusions.

Keywords: Adnexal surgery,benign uterine diseases, laparoscopic hysterectomy, laparotomic hysterectomy, gynecological surgery complication

INTRODUCTION

Hysterectomy refers to the surgical removal of the uterus and cervix, and salpingectomy and/or oophorectomy may be considered in the surgery. It seems the most frequently performed major surgery (about 600,000 times annually) following cesarean section (C/S) in the reproductive age in the United States.[1] About 68% of hysterectomies are performed by the abdominal route, most commonly with the indication of leiomyoma (40.7%). Moreover, oophorectomy is accompanied by hysterectomies at 53.8%.[1] It is known that 74% of hysterectomies are for benign indications.[2] It can be performed laparotomic (L/T), laparoscopic (L/S), robotic, and vaginal. The first planned successful vaginal hysterectomy was reported by Lagenbeck in 1817, subtotal abdominal hysterectomy by Kimball in 1855, and total L/S hysterectomy by Reich in 1989.[3,4] Despite vaginal and abdominal hysterectomy attempts until the aforementioned dates, high mortality rates were also reported due to indefinite surgical techniques, lack of vascular ligation, and failure to provide antisepsis.[3] Yet, L/S procedures have gained popularity compared to previous years.[2] However, abdominal hysterectomy still seems to be the most common surgical method despite more extended hospital stay, more postoperative pain, higher infection rates, and delayed return to everyday life.[5] The most common indications for L/T and L/S hysterectomies are leiomyoma and abnormal uterine bleeding, respectively.[6] Moreover, there may be many complications (e.g., infection, deep venous thrombus, gastrointestinal system injury, genitourinary system injury, and bleeding) during the perioperative period of hysterectomy.

The present study attempted to compare the difference between L/S and L/T hysterectomies and the addition of oophorectomy to surgery by complications, blood transfusion, and changes to hemoglobin (Hb) levels and explore the impacts of diabetes mellitus (DM), smoking, previous abdominal surgery, and body mass index (BMI) on early and late complications.

METHODS

This study was produced from the first author's specialization thesis in gynecology and obstetrics numbered 451277 and titled "Comparison of Laparotomy and Laparoscopy in Hysterectomies Performed for Benign Uterine Diseases."

İstanbul Medeniyet University, Goztepe Education and Research Hospital granted ethical approval to this retrospective cross-sectional study (Date: 01.02.2017 Decision no: 2016/0270). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

We first identified patients undergoing L/S and L/T hysterectomies for benign uterine indications between January 2012 and January 2017 from hospital records. After excluding endometriosis or malignant indications, adnexal masses, conversion from L/S to L/T, and vaginal and subtotal hysterectomies, we carried out the study with the data of 537 patients.

The patients were first divided into two groups: those with L/S (n=122) and L/T (n=415) hysterectomies. Then, they were further divided into four subgroups by oophorectomy. Accordingly, Group 1 had only L/S hysterectomy (n=30, 5.6%), Group 2 underwent L/S hysterectomy with oophorectomy (n=92, 17.1%), Group 3 had only L/T hysterectomy (n=108, 20.1%), and Group 4 was recruited for L/T hysterectomy combined with oophorectomy (n=307, 57.1%). We compared the main groups and subgroups by preoperative and postoperative sixth-hour Hb values (Δ1), preoperative and postoperative first-day Hb values (Δ2), intraoperative and postoperative blood transfusion, and early and late complications. We also evaluated the relationships between early and late complications and DM, previous abdominal surgery, smoking, and BMI in the groups.

We accepted complications occurring intraoperatively and till the end of the seventh postoperative day as early complications and those appearing on the eighth postoperative day as late complications.

Statistical Analysis

We utilized descriptive statistics to present the data. After ensuring the normality of distribution with the Kolmogorov-Smirnov test, we compared categorical data using the chi-square test and Fisher's exact test, while we utilized independent samples t-test and one-way analysis of variance (ANOVA) to compare the parameters between the groups. We ran the Tukey test in multiple comparisons to reveal the source of significant difference(s) between the groups. Moreover, we explored the associations between the continuous variables using Pearson's correlation analysis. All analyses were performed on SPSS 21.0, and a $p< 0.05$ at the 95% confidence interval (CI) was considered statistically significant.

RESULTS

We studied the data of 537 patients, 122 in the L/S group and 415 in the L/T group. We found the mean hospitalization length to be 2.710±0.955 days, the mean age to be 48.150±6.034 years, the mean body weight 71.100±9.460 kilograms, the mean BMI to be 26.820±4.273, the median gravida to be 4 (0-15), and the median parity to be 2 (0-10). Moreover, the findings showed the mean preoperative Hb value to be 11.949±1.441 gr/dL, the mean postoperative sixth-hour Hb value to be 10.931±1.320 gr/dL, the mean postoperative first-day Hb value to be 10.698±1.267 gr/dL, the mean Δ1 to be 1.036±1.037 gr/dL, and the mean Δ2 to be 1.268±1.070 g/dL. Besides, we discovered the subgroups had a similar distribution of BMI values (Group 1=26.0±3.92, Group 2=26.1±4.0, Group 3=27.1±4.4, Group 4=27.1± 4.3; p=0.198).

As indications for hysterectomy, we detected leiomyoma in 345 (62.4%) patients, abnormal uterine bleeding in 67 (12.5%), cervical intraepithelial neoplasia (CIN2, CIN3) in 21 (3.9%), adenomyosis in 39 (7.3%), endometrial pathologies (endometrial polyp, endometrial hyperplasia, tamoxifen use) in 64 (11.9%), and complete mole in 1 (0.2%) patient.

Table 1 shown comparisons of the main groups and subgroups by Δ1 and Δ2. We could not determine significant differences between the main groups and subgroups by Δ1 and Δ2 .

Table 1. Comparisons of the main groups and subgroups by Δ1 and Δ2

Main Groups				
	L/S (Group 1+2) (n=122)	L/T (Group 3+4) (n=415)	t*	p
Δ1	1.158±0.783	1.001±1.099	1.478	0.140
Δ2	1.274±0.748	1.267±1.149	0.082	0.935

Subgroups				
		M±SD	F#	p
Δ1			2.321	0.074
	Group 1 (n=30)	0.940±0.895		
	Group 2 (n=92)	1.229±0.734		
	Group 3 (n=108)	1.149±1.456		
	Group 4 (n=307)	0.949±0.939		
Δ2			1.162	0.324
	Group 1 (n=30)	1.160±0.839		
	Group 2 (n=92)	1.311±0.717		
	Group 3 (n=108)	1.421±1.502		
	Group 4 (n=307)	1.212±0.993		

Δ1: Difference between preoperative and postoperative sixth-hour hemoglobin values, Δ2: Difference between preoperative and postoperative first-day hemoglobin values, (*t-test, #ANOVA)

Table 2 shown blood transfusion and early and late complications between the main groups. We compared the main groups by intraoperative and postoperative blood transfusions and early and late complications. The findings revealed significantly higher postoperative blood transfusions in the L/T group compared to the L/S group.

Table 2. Blood transfusion and early and late complications between the main groups

	L/S (n=122)		L/T (n=415)		p
	n	%	n	%	
Intraoperative blood transfusion	2	1.6%	12	2.9%	0.445
Postoperative blood transfusion	1	0.8%	24	5.8%	0.022
Early complications	4	3.3%	14	3.4%	0.959
Late complications	4	3.3%	14	3.4%	0.959

Table 3 shown blood transfusion and early and late complications between the subgroups. We did not conclude significant differences between the subgroups by intraoperative and postoperative blood transfusions and early and late complications.

Table 3. Blood transfusion and early and late complications between the subgroups

	Group 1 (n= 30)		Group 2 (n=92)		Group 3 (n=108)		Group 4 (n=307)		p
	n	%	n	%	n	%	n	%	
Intraoperative blood transfusion	2	6.70%	0	0.00%	5	4.60%	7	2.30%	0.099
Postoperative blood transfusion	1	3.30%	0	0.00%	7	6.50%	17	5.50%	0.114
Early complications	1	3.30%	3	3.30%	6	5.60%	8	2.60%	0.542
Late complications	2	6.70%	2	2.20%	7	6.50%	7	2.30%	0.124

Among early complications, seven patients developed surgical site infections, six suffered bleeding requiring additional surgical intervention, and five had urinary system damage. As late complications, we detected surgical site infection in 13 patients, vaginal cuff hematoma in three patients, abdominal pain in one patient, and cuff cellulitis in one patient. A 48-year-old patient in the L/T group died of bleeding on the first postoperative day. Surgical site infection, accounting for 38% of early complications, 72% of late complications, and 55% of all complications, was found to be 3% among all patients. Moreover, hemorrhage requiring intervention and surgical-related hematoma, accounting for 33% of early complications, 16% of late complications, and 25% of all complications, were observed in 1% of all patients. Finally, 0.9% of all patients had urinary system damage, accounting for 27% of early complications, 0% of late complications, and 3% of all complications.

Early and late complications were addressed by DM, abdominal surgery, smoking, and BMI. 57 (10.6%) of 537 patients who underwent hysterectomy had a history of DM. Of the 18 early complications, 16 (3.3%) were detected in patients without DM and 2 (3.5%) in DM patients (p= 0.589). We also discovered that, among the 18 late complications, 17 (3.5%) were present in patients without DM and 1 (1.7%) in DM patients (p= 0.411). Moreover, 97 (18%) patients had a history of smoking. Our findings revealed early and late complications to be similar by smoking. Overall, 16 (3.6%) of early and late complications were found in non-smokers, while 2 (2.1%) were detected in smokers (p= 0.340). We discovered that 106 patients had a history of abdominal surgery once, and 59 patients underwent at least two abdominal surgeries. Early complications were observed in 13 (3.5%) patients without abdominal surgery, 4 (3.8%) with abdominal surgery once, and 1 (1.7%) with two or more abdominal surgeries (p=0.747). When it comes to late complications, the above findings appeared to be 14 (3.8%), 3 (2.8%), and 1 (1.7%), respectively (p =0.673). In general, we could not find significant differences among our patients in early and late complications by DM, smoking, and history of abdominal surgery. Besides, we calculated the mean BMI to be 26.82±4.30 for 519 patients without early complications and 27.03±3.50 for 18 patients with early complications (t=0.213; p=0.832). It was found to be 26.86±4.27 for 519 patients without late complications and 25.78±4.30 for 18 patients with late complications (t=1.056; p=0.292). Similar to the other parameters, the patients did not significantly differ in early and late complications by BMI.

DISCUSSION

Our findings revealed no statistically significant differences between L/S and L/T groups and between the subgroups by Δ1 and Δ2, perioperative blood transfusion, and early, late, and total complications. Despite no significant difference between subgroups by postoperative blood transfusion, postoperative blood transfusion requirement was significantly higher in the L/T group compared to the L/S group. Therefore, we can assert that the addition of an oophorectomy did not cause any additional risk. Moreover, we discovered that early and late complications did not significantly differ by DM, smoking, history of abdominal surgery, and BMI. Only one patient died of bleeding on the first postoperative day. Finally, there was surgical site infections in 3% of all patients, bleeding and hematoma requiring surgical intervention in 1%, and urinary tract damage in 0.9%.

Given the patient, surgeon, and hospital conditions, operators may prefer the vaginal route first, L/S second, and L/T third in hysterectomy patients. Salpingectomy can be safely adopted during vaginal hysterectomy.[7] While hysterectomy operations are often 'clean-contaminated,' they may become 'contaminated' in the case of perioperative urinary tract infection or bacterial vaginosis and 'dirty or infected in the case of purulent discharge due to intraoperative bowel perforation or pelvic inflammatory disease.[8] Febrile morbidity refers to body temperature above 38°C in at least two measurements at six-hour intervals starting 24 hours following the surgery. The most common infectious causes are known to be vaginal cuff cellulitis, infected hematoma or abscess, wound site, urinary tract, and respiratory infections. Preoperative antimicrobial prophylaxis depends on factors such as socioeconomic status, BMI, and concomitant procedures. In addition, high fever and leukocytosis can also be caused by non-infectious causes (e.g., atelectasis, hypersensitivity reactions, tissue trauma, or pyrogenic reaction to hematoma).[9] While the infection rate for abdominal hysterectomy is 10.5%, it is often reported to be 9% for L/S hysterectomy.[10] Compared to abdominal hysterectomy, there are lower febrile morbidity rates and fewer wound infections, while vaginal mold infection is higher in L/S hysterectomy.[11]

The ureteral injury is reported to be 1.6 (0-14.6) and bladder injury to be 2.6 (0.2-19.5) per 1,000 gynecological surgeries. Besides, 11.5% of intraoperative ureteral damage and 51.6% of bladder damage could be detected.[12] More urinary tract injury is reported in L/S hysterectomy.

Moreover, bladder, ureter, and urinary tract damage (bladder or ureter) is more common in L/S hysterectomy compared to L/T hysterectomy. Yet, intestinal damage is less in L/S hysterectomy.[11]

Compared to L/T hysterectomy, L/S hysterectomy has more vascular injury, less bleeding, and less pelvic hematoma and blood transfusion.[11] Similarly, more blood transfusion was needed in the L/T group in our study.

While the average hospital stay for abdominal hysterectomy is 3.07 days, it is 1.65 days for L/S hysterectomy.[13] Moreover, patients with L/S hysterectomy can return to their normal 15.17 days earlier compared to those with L/T hysterectomy.[11] A study reported that the rate of abdominal hysterectomy fell from 65% to 54%, while the rate of vaginal hysterectomy decreased from 25% to 17% in 2010 compared to 1998. Moreover, there was a decrease of 36.4% in the total number of hysterectomies in 2010 compared to 2002.[14]

In a study where more than 2 million benign hysterectomy cases were followed up between 1998 and 2006 in the USA, the addition of oophorectomy to vaginal hysterectomy increased complications (OR: 1.12, CI: 0.89-1.17), while there were no changes in abdominal (OR: 0.91, CI: 0.89-0.94) or laparoscopic hysterectomies (OR: 0.89, CI: 0.83-0.94).[15] Similarly, we could not concluded significant differences between L/S and L/T groups with added oophorectomy by complications, which may be because the operations may have been handled by experienced surgeons.

Obesity, DM, and smoking are prevalent risk factors for infection complications.[16-18] In this study, the fact that DM did not increase the risk of complications may have been due to tight perioperative glycemic control. In the preoperative stage, patients are recommended to quit smoking, and, therefore, many patients reduce their daily cigarette smoking. On the other hand, the fact that BMI showed similar distribution between the groups may not have had a significant effect on complications.

In our study, we discovered mortality in only one patient (0.18%). The previous research reported the mortality rate in abdominal hysterectomy to be 0.32-0.5 per 1,000 patients.[17-19] The present study is not free of a few limitations. Studying the data obtained retrospectively, considering operations performed by different operators, inequal numbers of patients in the groups, and lack of exact criteria for choosing the hysterectomy technique (L/S-L/T), and comparing operations for only benign indications may have created major limitations to this study. Moreover, the fact that the operations were performed by experienced surgeons with the help of advanced surgical techniques may have yielded similar complication rates in this study.

CONCLUSION

L/S hysterectomy may be preferred in relevant patients and indications since L/S and L/T hysterectomies demonstrate similar complication rates. The addition of an oophorectomy to either method seems not to contribute to complication risks.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of İstanbul Medeniyet University Goztepe Education and Research Hospital Hospital Ethics Committee study (Date: 01.02.2017, Decision No: 2016/0270).

Informed Consent: Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process: Externally peer-reviewed.

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Therapy options for psychiatric disorders in pregnancy

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ABSTRACT

While psychotherapy is often preferred in treating mild psychiatric disorders, drug and other non-drug options are adopted in treating moderate and severe conditions during pregnancy. In addition, cognitive behavioral therapy (CBT) has become prominent among psychotherapies. Regarding antidepressants, Sertraline, Citalopram, and Escitalopram are recommended as the first choices. Benzodiazepines are not recommended unless necessary; they are prescribed in the minimum dose and duration if highly needed. Mood stabilizers are considered risky and should be carefully used. Moreover, the expectant mother should be required for fetal follow-up more frequently and in detail when such drugs are prescribed. The safest among them is considered Lamotrigine. If antipsychotics are to be prescribed, the expectant mother's blood glucose, weight, and blood pressure should be followed up frequently. Due to the possible side effects to occur in the infant following delivery, antipsychotics may be considered to be discontinued immediately before birth and restarted after delivery. It is argued that there is no notable difference between the first and second generations. Besides, electroconvulsive therapy (ECT) is recommended in cases of suicidal depression, manic attack, psychotic attack, and catatonia where rapid response is required. Although promising results were previously reported about transcranial magnetic stimulation (TMS) and bright light therapy, their utilization areas are still limited.

Keywords: Pregnancy and psychiatric disorders, medication, non-drug therapy options

INTRODUCTION

Therapy options for psychiatric disorders during pregnancy are often divided into drug and non-drug therapies. While antidepressants, anxiolytics, mood stabilizers, and antipsychotics are presented as medication options, psychotherapy, electroconvulsive therapy (ECT), and transcranial magnetic stimulation (TMS) are adopted as non-drug therapies. They have also welcomed bright light therapy (phototherapy) oriented to depression in recent years. The level of the disorder is settled as mild, moderate, and severe by how much the psychiatric disorder disrupts functionality and daily life and by symptom severity. Psychotherapy often becomes prominent in mild conditions, while other drug and non-drug options are considered, as well as psychotherapy, in moderate and severe disorders.

DRUG THERAPY IN PSYCHIATRIC DISORDERS DURING PREGNANCY

Antidepressants

Selective serotonin reuptake inhibitors (SSRIs) are often the first choice when deciding antidepressants.[1] The literature hosts a plethora of studies on the use of these drugs for depression in pregnancy, and they were previously shown to be efficient. Despite conflicting findings on teratogenicity, the prevailing view is that they can be used at the minimum effective dose in case of indication; the risk of teratogenicity increases with increased doses.[2] A meta-analysis study concluded a 1.36-fold increase in the risk of a septal defect in the infants of 6.5 million expectant mothers using Sertraline in the first trimester, despite no association with other anomalies.[3] The previous research reported an increased risk of premature birth, persistent pulmonary hypertension, and neonatal adjustment syndrome both in sertraline use and untreated pregnancy depression.[4] In addition, the risk of neonatal seizures was found to be higher when using tricyclic antidepressants.[5] However, there is growing evidence that Sertraline, Citalopram, and Scitalopram are relatively safe. Paroxetine was found to be riskier for cardiac anomalies. Fluoxetine is, on the other hand, a drug with a long half-life. Therefore, these two drugs are not recommended as the first choice but can be started after informing the expectant mother and her relatives in the case of no response to the others and a history of response to them.[6]

It is suggested that tricyclic antidepressants should not be the first choice because of the risk of teratogenicity and side effects.[7]

Despite not satisfying data on Mirtazapine, it is suggested to be used in the case of hyperemesis, insomnia, anorexia, and weight loss.[8]

Some studies reported no increase in the risk of anomalies related to Venlafaxine and Duloxetine, the members of SNRIs, but further research is needed on this subject. Venlafaxine may increase the risk of hypertension; therefore, it should be avoided in high-risk pregnancies in terms of preeclampsia-eclampsia.[9]

In the postpartum period, the first choice for breastfeeding mothers is Sertraline and Paroxetine, which are known to pass into milk the least. Other SSRI drugs can also be used in the case of no response to the above-mentioned options or emerging intolerable side effects.[10]

Anxiolytics

Benzodiazepines cross the placenta. The use of Benzodiazepines during pregnancy was found to be associated with anal atresia and cardiac anomaly,[11] low birth weight and preterm birth,[12] drowsiness, reduced muscle tone, and decreased feeding when used close to birth and neonatal withdrawal syndrome, somnolence, irritability, difficulty sucking, tremor, tachypnea, gastrointestinal symptoms, hypoglycemia, and hypothermia among ¼ of babies during late pregnancy.[13,14] Although it was considered a teratogen for a while until further research on the grounds that it might cause cleft lip and palate,[15] the current studies established no relationship between major malformations and Benzodiazepine use. While some studies suggested that Benzodiazepines should be gradually tapered and discontinued until delivery to avoid possible postpartum complications, some others opposed such a suggestion because the mother's anxiety symptoms may also increase.[16] As a result, the use of benzodiazepines is not recommended during pregnancy. Only limited use is recommended for the lowest dose and duration in severe anxiety attacks and sleep disorders that do not respond adequately to non-drug therapies and antidepressants.

Since the data on the use of beta-blockers during pregnancy were obtained from expectant mothers using them for hypertension and cardiovascular reasons, it is unclear whether the fetus-specific effects are due to medical reasons or drugs.[17] Yet, they are accepted as non-teratogens.[18] Some studies suggested they are associated with feeding problems, hypoglycemia,[19] low birth weight, and hemodynamic disorders in infants.[20] Overall, although they are not considered teratogens, it is proposed that they may have adverse effects on the infant in the postnatal period.

Antihistamines are used for allergy and hyperemesis during pregnancy, and those with low sedation effects are preferred. The literature lacks research on its use for anxiolytic and hypnotic purposes.[21] Diphenhydramine, Cetirizine, and Hydroxyzine were not found to be associated with a malformation.[22]

Although it was shown that the use of Pregabalin and Gabapentin during pregnancy does not contribute to the risk of malformation, they are not recommended to be used because not only was the number of relevant studies limited but also a study with a smaller sample concluded contrasting findings study.[23,24]

Mood Stabilizers

Lithium is a drug with placental transfer used as a maintenance therapy during remission to alleviate acute attacks (hypomania, mania, depression) and prevent attacks in bipolar disorder. The blood lithium level is the same in the mother and the fetus, but its half-life is longer in the fetus since the fetus' renal clearance will not be sufficient; therefore, it should be considered that lithium may reach toxic levels in the fetus. Ebstein Anomaly was found 400 times more in babies exposed to lithium in the first trimester.[25] Its use between 2-6 weeks was found to be riskier, and subsequent studies concluded the risk to be 20-40 times lower.[26,27] Another study discovered a three-fold increase in all congenital malformations and an eight-fold increase in cardiac anomalies.[28] On the other hand, a relatively recent review mentioned that it would not contribute to the risk of major malformations.[29] In the literature, complications that are uttered to be linked with lithium use during pregnancy are listed as preterm birth, high birth weight, nephrogenic diabetes insipidus, hydramnios, floppy baby syndrome, transient neurodevelopmental defects, poor newborn reflexes, apnea and respiratory distress, feeding difficulties, bradycardia, thyroid dysfunctions, and low birth weight. High-resolution ultrasonography and fetal echocardiography are recommended for expectant mothers using lithium between 16-20 weeks of pregnancy. Since the blood volume may decrease, reducing the lithium dose before delivery is also recommended to prevent possible toxic effects in pregnant women using lithium. Another recommendation is to discontinue lithium two days before delivery and restart it after delivery.[30] Overall, a considerable number of studies recommend that lithium should not be used in the first trimester unless mandatory and should be discontinued just before delivery and restarted after delivery.[31]

A meta-analysis study on valproic acid showed an increased risk of spina bifida, atrial septal defect, cleft palate, hypospadias, polydactyly, and craniosynostosis when it is used in the first trimester of pregnancy. Even the risk increases much more when the daily dose exceeds 1000 mg.[32] Irritability, feeding problems, reduced muscle tone, liver toxicity, coagulopathy, and hypoglycemia were previously reported in infants exposed to valproic acid close to birth.[33] Intramuscular vitamin K should be administered just before delivery to reduce the risk of coagulopathy.[34] Overall, it can be asserted that the use of valproic acid should be avoided during pregnancy if possible. If only valproic acid has benefited so far and the symptoms increase when discontinued, patients are recommended to use it at a lower dose.[31] Moreover, starting folic acid supplementation before pregnancy is recommended to reduce the risk of neural tube defect development among patients with a pregnancy plan who are recommended to continue with valproic acid during pregnancy.[34]

Carbamazepine was formerly considered a teratogen; nevertheless, current data propose vice versa. It increases the risk of congenital anomaly (3-6%) but is thought to be safer than valproic acid.[34] Neural tube defects, cleft palate, cleft lip, cardiovascular anomaly, products system anomaly, short nasal root, hypertelorism, and fingertip hypoplasia

were reported in the case of Carbamazepine use.[35] Folic acid supplementation is also recommended for expectant mothers to use Carbamazepine.[31]

Lamotrigine is safer than other mood stabilizers; the risk of malformation is 2-3%. Although an increased risk of cleft palate and lip, hypospadias, and gastrointestinal defects were mentioned, no dose-dependent relationship was previously detected.[36]

Antipsychotics

Apart from the possible teratogenic effects related to the use of antipsychotics during pregnancy, another risk that may arise in all antipsychotics, particularly those of the second generation, may be the complications such as increased appetite, weight gain, insulin resistance, hyperglycemia, hypertension, obesity, and gestational diabetes.[37]

In the second generation, Clozapine and Olanzapine are the riskiest drugs for gestational diabetes. However, Risperdal carries a relatively lower risk. Moreover, the previous research could not conclude a relationship between risky situations in pregnancy and the use of Amisulpride, Aripiprazole, Quetiapine, Sertindole, and Ziprasidone.[38]

Although the use of first-generation antipsychotics is gradually decreasing, Haloperidol and Chlorpromazine are still preferred and have been used safely at low doses for years in the treatment of hyperemesis gravidarum. In addition, no risk of teratogenicity was mentioned in the literature.[39]

A study on the use of antipsychotics during pregnancy reported an increased risk of gestational diabetes, preterm birth, and low birth weight. In the same study, it was mentioned that the use of antipsychotics during early pregnancy may cause an increase in the risk of atrial and ventricular septal defects and that any relationship could not be established clearly due to confounding factors such as concomitant use of other drugs.[40]

Two recent reviews on the subject complained about insufficiency and reported no relationship between the use of antipsychotics during pregnancy and congenital anomalies.[41]

The British Association for Psychopharmacology's guide on the use of psychotropics during pregnancy mentions a moderately increased risk of complications (e.g., congenital anomalies, preterm birth, developmental disorders, and newborn adjustment problems) among women using antipsychotics during pregnancy than healthy women. It also reports a low degree of risk when compared to pregnant women who have a psychiatric disorder but do not use medication. Besides, it utters no difference between the first- and second-generation antipsychotics by fetal risk when considered at the class level or individually.[42]

In another study, the authors reported no relationship between the use of antipsychotics during pregnancy and a major congenital anomaly. Neurodevelopmental and behavioral disorders were significantly more common in the infants of women having used antipsychotics compared to those of women who did not. Yet, the statistical significance was lost when confounding factors (e.g., smoking, alcohol, substance use, and concomitant use of other drugs) were controlled.[43]

A previous meta-analysis study revealed a relationship between antipsychotic use during pregnancy and congenital anomalies, preterm birth, low birth weight, and elective curettage but noted that this relationship might be doubtful due to confounding factors. However, the authors could not conclude such a relationship between the first- and second-generation antipsychotics and highlighted that and the multitude of confounding factors (e.g., smoking, alcohol and substance use, obesity, socio-economic problems, concomitant use of other drugs and excess medical comorbidities) among expectant mothers using antipsychotics limited the research findings.[44]

A reasonable order among antipsychotics by placental transfer may be as follows: Olanzapine > Haloperidol > Risperidone > Quetiapine.[45]

Extrapyramidal manifestations were observed in the infants of mothers having used antipsychotics close to delivery. Due to the risk of neutropenia in the infants of mothers using Clozapine, it is recommended to follow up hemogram once a week in the first month and then once a month for six months after delivery.[38]

NON-DRUG THERAPIES FOR PSYCHIATRIC DISORDERS DURING PREGNANCY

Cognitive Behavioral Therapy (CBT)

CBT is one of the main schools of psychotherapy and has become widespread worldwide in the last 50 years. It is also among the leading non-drug therapies for expectant mothers with mild depressive and anxiety disorders with no severe symptoms. The relevant literature hosts a plethora of studies showing its efficacy and safety. It is an evidence-based and structured psychotherapy method and the first-choice therapy for those afraid of drug exposure and with drug rejection. While it can be administered to expectant mothers already exhibiting mild symptoms, it can also be preferred prophylactically for women expecting pregnancy with a history of depression and anxiety disorder. Interventions with CBT for distorted cognitions (e.g., inadequacy, guilt, inability to cope, and catastrophizing) are recommended to prevent or mitigate the disorder that may occur during pregnancy. It was consistently shown to be as effective as medication in depression with mild symptoms and no psychotic symptoms.[46]

Electroconvulsive Therapy (ECT)

It is the stimulation of the brain with a low electrical current and having a seizure. Although the mechanism of action of which has not been clarified despite being utilized in psychiatry for a long time, it is a reliable therapy with a rapid response, proven efficiency in some psychiatric disorders, and several advantages in terms of side effects.

ECT is indicated in cases with moderate and severe depressive episodes (unipolar or bipolar disorder), no response to the drug, suicidal risk, insufficient nutrition (malnutrition or dehydration), psychotic symptoms, signs

of agitation and catatonia, no cooperation, and treatment rejection. According to a meta-analysis, ECT was found to be more effective than drug therapy and imitation ECT in depression.[47]

Apart from this, manic episodes (bipolar disorder), psychotic exacerbation (schizophrenia, schizoaffective disorder), and catatonic symptoms for whatever reason, bear ECT indications during pregnancy.

The most common side effects in the mother following ECT during pregnancy are transient and mild nausea-vomiting, muscle pain, and headache. The most prominent undesirable side effects are uterine contractions and premature birth, observed at a frequency of 3.5%. The current does not pass through the uterus, which is thought to be related to oxytocin release during ECT. Its side effects on the fetus are reported as transient cardiac arrhythmias, and its relation with congenital anomalies was not reported before.[48]

Drugs increasing the seizure threshold (e.g., benzodiazepines and mood stabilizers) should be discontinued a few days before ECT.

Transcranial Magnetic Stimulation (TMS)

Whereas it lacks enough data to be utilized as the first-choice therapy, it can be considered in selected cases. It is a novel method deployed leading to neurotransmitter release by stimulating neurons with magnetic stimulation (neural depolarization) in various neurological and psychiatric disorders. Concerns about drug exposure and myths about ECT have highlighted this method in recent years. The literature hosts only three studies conducted so far showing its efficacy and safety in the treatment of depression in pregnancy, and any of these studies reported no serious side effects. The most common side effect was reported to be a headache at a rate of 40%, and all infants were born healthy.[49] Previous research on the non-pregnant anxiety disorder population demonstrated that it can be reliably utilized in anxiety disorder during pregnancy despite no study yet on its efficacy and safety among expectant mothers.[50]

CONCLUSION

Psychiatric disorders often occur in the reproductive age between 18-45 years in women. Therefore pregnancy is a period of increased susceptibility to psychiatric disorders such as anxiety disorders, depression, eating disorders, and psychosis for many women. In this article, psychiatric disorders in pregnancy and lactation period and treatment options are reviewed in light of current treatment guidelines. The benefits, teratogenicity risks of psychopharmacological treatment during pregnancy should be considered carefully. The lowest effective dose and single medication should be used, and fetal / infant must be closely monitored during pregnancy.

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Montessori education: an expert view

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ABSTRACT

The present study aims to delineate Montessori education relying on the review of current literature. Given the background of early childhood education, this method dates back to the early 19th century, and the most influential educator in this method is undoubtedly Maria Montessori. She is an educator having devoted her life to improving the education system for children and is the first female medical doctor in Italy. The years characterized by wars and poverty led her to engage in observation of the education of mentally retarded children and, thus, laid the foundations of an influential education model across the world. She opened her very first school, the Casa Dei Bambini (Children's Home), in Rome in 1907. Today, her education model can be considered among the ones preferred the most and is adopted within both private and public schools in our country.

Keywords: Montessori, child education, cognitive development

INTRODUCTION

The first six age can be conceived as a period that influences human life the most and when the child's personality traits and emotional and physical development are shaped the fastest. It can be proposed that a child is born with a specific genetic potential, which can be utilized to the fullest only with the appropriateness of the environment and support.[1] Educational activities for children aged 0-6 are called preschool education, highly acknowledged by developed and developing countries through adopting diverse methods.[2]

In the preschool period, play is the child's fundamental and indispensable occupation. Play also holds a key role in the child's physical, physical, psychomotor, cognitive, emotional, and social development. What nurtures the child's soul the most may be the play, following affection. Play liberates the child and increases their desire to learn. Thus, movement and play are two essential keywords describing young children.[3]

The sense of self in childhood emerges when starting walking, while the ages of 3-6 are defined as the period of curiosity and assertion. In this period, criticism and intimidation may hinder their assertive power. Consequently, the child that feels worthless begins to develop an insecure self.[4]

Children need support, opportunities, and freedom without harming the environment and themselves to be able to perceive that they can succeed in their behavior. Besides, a substantial part (80%) of the child's mental development is achieved in preschool.[5]

MONTESSORI EDUCATION

Given the background of early childhood education, this method dates back to the early 19th century, and the most influential educator in this method is undoubtedly Maria Montessori. She is an educator having devoted her life to improving the education system for children and is the first female medical doctor in Italy. The years characterized by wars and poverty led her to engage in observation of the education of mentally retarded children and, thus, laid the foundations of an influential education model across the world. She opened her very first school, the Casa Dei Bambini (Children's Home), in Rome in 1907. Today, her education model can be considered among the ones preferred the most and is adopted within both private and public schools in our country.[1]

Montessori especially emphasizes that every child is unique; therefore, education should be individualized, and respect for the child needs to be adopted as the most important principle. In this sense, the child should be allowed to do their own work and learn by themselves. The second principle refers to the first three years of age, when the child's brain acquires all the fundamental knowledge like a sponge. The child also learns by watching the environment. The third significant principle assumes that there are sensitive periods when the child learns specific behaviors more easily. Although these periods differ by child, parents and educators may have to support their development continuously in these periods.[1]

Montessori often states that tailored-made environments need to be created for children to learn and develop, to become independent of adults, and to enjoy opportunities. Household items in their own size and designing rooms in

such a way that children reach everything are also among the basic principles.[1]

The most obvious feature of Montessori's Children's House is that the furniture is designed to be suitable for children's sizes. In this way, children do not need to ask for adult help. They only need supportive help since their development will be hindered and traumatized if their parents do everything for them.[6]

Two prominent features of the child's soul are that they are busy with a task and do it with a sense of achievement. The child's most significant job is to imitate adults. Their effort to gain independence is also appreciated. As the child sees their own achievement, they will definitely enjoy it and develop, such as giving the child a small mirror and brush to comb their hair or having bathroom items suitable for their height to allow them to wash their hands on their own. While doing their own work, the child may also request support from the teacher. Therefore, parents or teachers must learn to be patient and wait while the child does their work. Providing the child with the necessary support, not too much, and giving unnecessary help should be stopped since this method relies on self-learning.[7]

MONTESSORI CLASSROOM AND MATERIALS

Montessori Children's House accepts children from the age of 2.5-3 up to 6 years. Following birth, the child shows rapid physical development till the end of 2 years. What is most evident is that their mental development is initiated and progresses in this period. The child hears, sees, smells, touches, bites, and, thus, learns about the outside world.[8]

The child often loves to perform an activity as a whole. It gives the child a sense of power and independence for succeeding, no matter how insignificant to an adult. In other words, success brings happiness, and happiness brings repetition and motivation, which is the most fundamental rule in Montessori schools. It is also the case in physical motor development (sitting, turning, stepping, walking). The child attaches pretty much importance to order; repeating some games or movements for a long time both calms them down and makes them happy.[9]

Montessori schools have free, supportive environments for children to do their own chores. Daycare centers primarily offer activities of daily living where the child can try them out on their own to learn (e.g., dressing baby up, undoing knots, putting on keys, unlocking, arranging dinner table, removing dishes, etc.).

The child's growth occurs in developmental stages. Each developmental stage affects all the next stages and loses its importance when the child begins to learn new things. The child must act in the direction where nature pushes them. Thus, if the child is not offered opportunities or they are not supported, they will probably begin to demonstrate abnormalities. The child whose work is inhibited may be psychologically hurt, or the child who is constantly interfered with gradually loses their courage, consistency, and determination. Hence, parents must consider it while raising their children.[10]

In Montessori schools, the teacher clearly shows activities to the child, and they try to do them on their own. The teacher may help the child if they ask for it, but the teacher does not do their activities on behalf of the child. If the child is often hindered when starting an activity, their inner motivation is ruined, leading them to think, "If I start this activity, someone will stop me, then I will not start it." Thus, the child's unconscious mind develops carelessness, discouragement, hesitancy, and indecision. They may constantly be afraid of being hindered, loses the courage to complete what they have started, and ends up with an inferiority complex. At the end of the story, the child's intelligence and ability are ruined. A general characteristic of children with strong characters who cannot put their minds and actions in order is that they get angry quickly. A messy mind, erratic movements, and anger go together. It is easy to suppress the child, but what is difficult is to prepare an environment where they can show wholesome development.[11]

The child's ability to observe and explore plays a role in their learning. The child, who is completely busy shaping their own personality before the age of 2.5 years, does not even play with their peers. Yet, they love to be in the environment and socialize by the age of 2.5-3 years. The child, then, needs to be helped in their journey of observation and discovery. For this, it is necessary to tell the child where to go, to make the preparations together, and to walk with them (not in the stroller) in nature at their pace. They will probably be interested in the environment in this process and look, examine, and explore plants and insects for minutes.[12]

Scholars working on child psychology often focus on the development of the child's ability to imitate, play, and imagine. In the early years, they investigated the impacts of external factors on child development, yet they discovered that the child's mind could do much more than anticipated. Montessori was also among those realizing that the child's learning ability to learn varies by their age. These sensitivity periods were also noticed, particularly in language and vocabulary learning. It was discovered that a 3.5-year-old child can incredibly acquire what they hear and looks at and quickly memorize the books read to them, the drawings of friends. In this regard, Montessori emphasizes the importance of teaching children the words about facts, geometric objects, geography, animals, and plants. The previous research documented that a 3.5-year-old child can learn the above-mentioned concepts more easily than a 5-year-old child.[13]

There is a plan to which the universe is entirely subject, and everything in nature continues its development in accordance with its own development law. The urge to protect offspring and preserve the kind is certainly one of the strongest urges in nature. Every living thing in nature has duties for the common good of the universe, apart from following the route of its own lineage. The secret of a happy life lies in pleasant works. While playing with toys at home, the child should be shown the fine details of playing gently and observed only for their own dealing, saying, "You can do it, too." It is the respect to the child to do activities they are interested in with them. Yet, they need to be explained and shown the limits against their actions to harm themselves, the environment, or an object.[14]

Since the child's learning of adult life should be like playing a game, it may be helpful for them to use brooms, cloths, jugs, glasses, and spoons suitable for their size at home. Games and activities should always be staged from easy to difficult to ensure eye-hand coordination and control. It is important for the child to do something willingly and by trying, and each child's development is unique. In this sense, Maria Montessori always adopts the ideas of freedom and independence in the education of children. The child learns to be independent of the parents taking care of, feeding, and dressing them so that they can exhibit their inner nature, which, in turn, grants them freedom. Those responsible for raising the child should allow them to learn and do and should not serve them not to leave the child dependent on them. The child is weaned and begins progressing on the risky path of absolute independence. In this path, one needs to remember that a person with too many servants becomes a slave to the servants as a result of becoming more and more dependent on them. Or else, the child may turn into one with no desire to make an effort, ruined capacity, weak mentality, and insensitivity. When a person, who has always been served, suddenly awakens one day and wants to gain independence, they will perhaps find that they no longer have the strength to do so, which is what wealthy families should not forget.[15]

Materials for Daily Living Skills Development

Both physiological and psychological development spring from a single source, life. One sometimes needs not to stain and smother the hidden potential of life but wait for it to unfold itself. Montessori children perform activities called "daily living skills" with astonishing calmness and dignity. There are also materials for teaching emotions, tools, alphabet, numbers, reading and writing, and four operations for the development of the child's mind while learning to use the items used in daily life. The teacher entirely teaches the use of all materials. The use of objects teaches order in the environment. Then, the child is free and makes their choice.[16]

It is critical to refer to nature to raise awareness among children who only enjoy the moment. The child, who knows that animals need human care and that a plant withers and dies when not watered, connects today's memories with a bond of affection to the future. The observations by Montessori for years imply that especially children free in their choices can extract different outcomes from their own thoughts. For example, she discovered that the child participating in the fruit or grain harvest later worked more willingly at the planting time.[17]

Child's Discovery

The toys around the child (at school or home) must be under the control of the material called "Control of Error." For example, it applies to the activity of "knobbed cylinders." A cylinder not put in its actual place will eventually cause several cylinders to be left at the top, or a sequencing error in button fastening will leave one button exposed. Thus, the child realizes the error and achieves perfection by repeating it. Controlling the errors through materials leads the child to use their mind, critical ability, and capacity to see distinctions.

The fact that educational materials are mobile, reusable, and relocatable increases their attractiveness. It is undoubtedly that an attractive toy or a picture attracts the child's attention, but of a shorter span. In the application of Montessori educational materials, it is critical that the child recognizes their limits. The child's mind always seeks to explore the environment and what is new. In other words, the presence of excessive toys and educational materials in the environment will cause distraction and confusion, leading them to lose their enthusiasm.

There are many educational materials in Montessori schools besides activities of daily living. Children are provided to see, feel, and perceive differences in learning. The fact that the differences are primarily opposites is also the basis of the learning steps. The child, who perceives the difference between a flat surface and a rough surface, can then understand their subtle differences, which also applies to materials with weight, size, and sound differences.

When it comes to colors, for example, the child learns red and yellow first in matching or ordering slightly different materials. The entire order is shown in the activities from left to right and top to bottom, which may be a simple guide to the Latin alphabet. Montessori schools have exclusive materials for visual object education: knobbed cylinders, red sticks, pink towers, brown ladders, color tablets, and geometric shapes.

There may be mistakes in playing with the materials in Montessori schools, but the child sees the mistakes themselves while playing and finds the right by repeating it; the aim is to learn by mistakes. Finally, everyone applies the rule of putting the materials in their places.

The teacher must teach objects to the child, which consists of three stages. First, the object is shown clearly, its name is called, and the object and its name are coded in the brain. Second, the child has to find and show the object when its name is called. Finally, all learning stages are performed simultaneously by asking the child, "Can you show me the blue ball?" and "What is this?"

CONCLUSION

Montessori education is a curriculum-oriented method to realize the child's inherent desire to learn instead of imposing knowledge on the child. Montessori education and materials are through to make significant contributions to the child's development and learning. The teacher's task is to guide the child; it would be inappropriate to be too intrusive or ignore everything.

In this sense, for Montessori education in the preschool period:

- children should be encouraged to research, communicate, and learn by allowing them to move freely in the educational environment. Moreover, relevant bodies may put efforts into disseminating Montessori education.
- theory and practice books covering Montessori practices can be prepared for preschool education.
- the curricula adopted in preschool education institutions can be enriched with Montessori education practices.

ETHICAL DECLARATIONS

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