İSTANBUL ÜNİVERSİTESİ YAYINEVİ

RESEARCH / ARAŞTIRMA
DOI: 10.26650/IUITFD.2020.0001
İst Tıp Fak Derg 2020 / J Ist Faculty Med 2020

INCIDENCE OF HYDATIDIFORM MOLE IN SYRIAN IMMIGRANT WOMEN AND TURKISH WOMEN

SURİYELİ GÖÇMEN VE TÜRK KADINLARINDA HİDATİFORM MOL İNSİDANSI

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Cite this article as: Erkinuresin T, Demirci H. Incidence of hydatidiform mole in Syrian immigrant women and Turkish women. J Ist Faculty Med 2020;83(4):427-33. doi: 10.26650/IUITFD.2020.0001

ABSTRACT

Objective: Immigration may affect the incidence of hydatidiform mole (HM). In this study, we aim to compare Syrian immigrant and Turkish pregnant women in terms of HM due to abortion and termination of pregnancy.

Method: An analysis of 907 endometrial curettage materials due to abortion or termination of pregnancy between the years 2016-2018 were performed. These curettage materials were examined with routine histopathologic methods. Examination of the curettage materials was repeated by a pathologist to confirm the diagnosis.

Results: HM was diagnosed in 56 of 768 Turkish pregnant women (7.30%) and it was diagnosed in 22 of 139 Syrian immigrant pregnant women (15.80%). HM incidence in Syrian immigrant pregnant women was significantly higher (2.06 times) than in Turkish women (p=0.001). The rate of Syrian pregnant women in the group aged 20 or younger was significantly higher than Turkish pregnant women (p<0.001). The rate of Turkish pregnant women aged between 30-34 and older was high in the group.

Conclusions: The incidence of HM is higher in Syrian pregnant women. The main causes affecting the incidence of HM in Syrian immigrants are nationality and age. Migration, with all its components, may explain the difference in HM incidence between these two neighboring communities.

Keywords: Adolescent pregnancy, dilatation and curettage, histopathology, hydatidiform mole, Syrian refugee

ÖZET

Amaç: Göç hidatiform mol (HM) insidansını etkileyebilir. Bu çalışmada, küretaj uygulanan ve gebeliği sonlandırılan Suriyeli göçmen ve Türk gebe kadınların HM açısından karşılaştırılması amaçlanmıştır.

Yöntem: 2016-2018 yılları arasında küretaj uygulanan ve gebeliği sonlandırılan 907 endometriyal küretaj materyalinin analizi yapıldı. Bu küretaj materyalleri rutin histopatolojik yöntemlerle incelendi. Küretaj materyallerinin incelenmesi, tanıyı doğrulamak için bir patolog tarafından tekrarlandı.

Bulgular: HM, 768 Türk gebe kadından 56'sında (%7.30) ve 139 Suriyeli göçmen gebe kadından 22'sinde (%15,80) teşhis edildi. Suriyeli göçmen gebe kadınlarda HM insidansı Türk gebe kadınlara göre (2,06 kat) anlamlı derecede yüksekti (p=0.001). Yirmi yaşından küçük olan gruptaki Suriyeli gebe kadınların oranı Türk gebe kadınlara göre anlamlı olarak daha yüksekti (p<0.001). Türk gebe kadınların oranı ise 30-34 yaş ve daha yaşlı olan grupta yüksekti.

Sonuç: Suriyeli göçmen gebe kadınlarda HM insidansı daha yüksektir. Suriyeli göçmenlerde HM insidansını etkileyen başlıca nedenler milliyet ve yaştır. Göçmenlik tüm bileşenleri ile bu iki komşu topluluk arasındaki HM insidansındaki farkı açıklayabilir.

Anahtar Kelimeler: Adolesan gebelik, dilatasyon ve küretaj, hidatiform mol, histopatoloji, Suriyeli göçmen

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Submitted/Başvuru: 15.01.2020 • **Revision Requested/Revizyon Talebi:** 14.04.2020 •
Last Revision Received/Son Revizyon: 18.04.2020 • **Accepted/Kabul:** 29.06.2020 • **Published Online/Online Yayın:** 05.10.2020

INTRODUCTION

There has been intense immigration towards Turkey from Syria since 2011 due to the ongoing conflict in Syria. The Ministry of Internal Affairs Directorate General of Migration Management declared that the total population of Syrian refugees in Turkey registered by their biometric data as of 8th November 2018 is 3 million 594 thousand 232 (1). 1 million 950 thousand 182 of these refugees are male and 1 million 644 thousand 50 of them are female (1). Syrian refugees benefit from health services in our country free of charge. According to official records, 276 thousand 158 Syrian babies were born in Turkish hospitals from 2011, when Syrians first started to enter the country, until 11th December 2017 (2).

Unintended pregnancy is of high incidence among the immigrant population. Termination of unintended pregnancy is legal until the 10th week after conception. After 10 weeks of pregnancy, abortion can only be performed in case of fetal impairment. Abortion is performed in pregnant women with findings of hydatidiform mole (HM) existence based on their human Chorionic Gonadotropin (hCG) levels and ultrasonography examination (USG) during periodic pregnancy follow-ups. HM is one of the diseases caused by villous trophoblasts associated with pregnancy (3). The most benign disease among gestational trophoblastic diseases is HM (4). HM has two histological types, partial hydatidiform mole (PHM) and complete hydatidiform mole (CHM) (5). hCG levels of CHMs are usually over 100,000 mIU/mL and fetal heart sounds do not exist (6-9). hCG levels are over 100,000 mIU/mL in less than 10% of PHMs (10-12).

HM prevalence varies throughout the world and occurs between 0.3 and 2.0 in one thousand pregnancies (5, 13-15). HM prevalence in curettage materials due to abortion or termination of pregnancy varies between 2.2% and 6.9% (3, 12, 27). There is proof that the incidence of HM has been decreasing in all societies in the last 30 years (16, 17).

Two risk factors detected in CHM development are advanced or early maternal age and previous molar pregnancy (18, 19). When compared to women aged between 21-35, women older than 35 and younger than 21 have a 1.9-fold increase in risk of CHM. Women older than 40, experience a 7.5-fold increase in risk (18, 19). Risk of HM pregnancy following another HM pregnancy is more than 10-20-fold higher depending on the society (20, 21). Another risk factor for HMs is spontaneous abortion history. This situation poses a risk of HM pregnancy of more than 2-3-fold higher depending on the society (22). Moreover, the age of menarche, parity, the time between previous pregnancies, genetic factors, malnutrition, viral infections and low socio-economic level provide predisposition for gestational trophoblastic diseases (GTD) (23). It is also detected that there is a reverse relationship between HM and the existence of ß-carotene and animal-fat in the diet (24, 25).

In this study, we aim to compare Syrian immigrant and Turkish pregnant women in terms of HM incidence in endometrial curettage materials performed due to abortion and termination of pregnancy in a tertiary hospital.

METHOD

Ethics committee approval for the study was obtained from the ethics committee for clinical research of our institution. Pathology reports of 907 endometrial curettage materials performed due to abortion or termination of pregnancy between the years 2016-2018 were digitally analyzed. Cases were evaluated retrospectively in light of the information obtained from pathology reports. Cases were classified as Syrian or Turkish. Cases with HM were compared in terms of age and incidence of the disease.

Curettage materials submitted to our pathology laboratory due to abortion or termination of pregnancy were examined with routine histopathologic methods (Hematoxylin & Eosin staining). Examination of the curettage materials was repeated by a pathologist to confirm the diagnosis.

In light of the histopathological findings described below, we diagnosed HM (partial or complete).

Microscopic examination shows a mixture of two villus populations consisting of small, fibrotic and normal-looking villi with large, irregularly shaped, slightly synsityotrophoblastic hyperplasia followed by hydropic villi in partial HM (Image 1). In some large villi, cisternae (cavitation) can be seen, while other large villi appear dysmorphic with their irregular scalloped complex contours and their

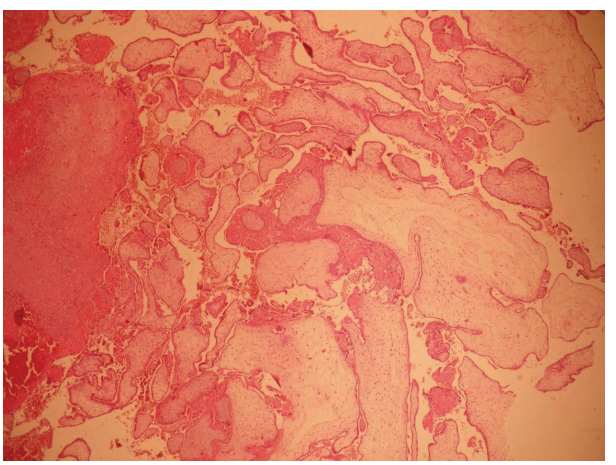

Image 1: Microscopic examination shows a mixture of two villus populations consisting of small, fibrotic and normal-looking villi in partial HM and large, irregularly shaped, slightly synsityotrophoblastic hyperplasia followed by hydropic villi. Cisterns (cavitation) can be seen in some large villi, while other large villi appear dysmorphic with their irregular scalloped complex contours and their invaginations and inclusions paved with trophoblasts. 10X H&E.

invaginations and inclusions paved with trophoblasts (Image 1 and 2). Generally, mild villous and chorionic plate trophoblast (predominantly synsityotrophoblastic) hyperplasia is seen. There is usually no apparent cytological atypia in trophoblasts. They also often contain fetal erythrocytes with villous blood vessels nucleus. Other evidence of fetal development (embryonic or fetal tissue, chorionic membrane, amnion, yolk sac, and umbilical cord) can also be seen.

In complete HM, the lesion consists entirely of large, hydropic and often cisternal villi. In addition, the common trophoblast layers that combine one or more villi and encircle the villi are also a distinct finding. The concentric distribution of this villous trophoblastic proliferation to some villi and the formation of both cytotrophoblasts and syncytiotrophoblasts is also a remarkable finding. Usually, syncytiotrophoblasts may appear immature and form Medusa-like festoons that emerge from molar villi (Image 3). There is also a marked trophoblastic atypical especially in the decidual implantation area (Image 4). Non-villous gestational tissues (embryonic or fetal tissue, chorionic membrane, amniotic, yolk sac, and umbilical cord) and fetal erythrocytes with nucleus are typically absent. Despite all these histopathological findings, in some early cases, the complete HM may be confused with partial HM. P57 immunohistochemical examination may be useful in this distinction. Nuclear staining is seen in trophoblasts that lay villi in partial HM, while no staining is seen in complete HM (Image 5).

Normal distribution suitability of variables was analyzed with the Shapiro Wilk test. Age as a result of the normality test is expressed as mean ± standard deviation and

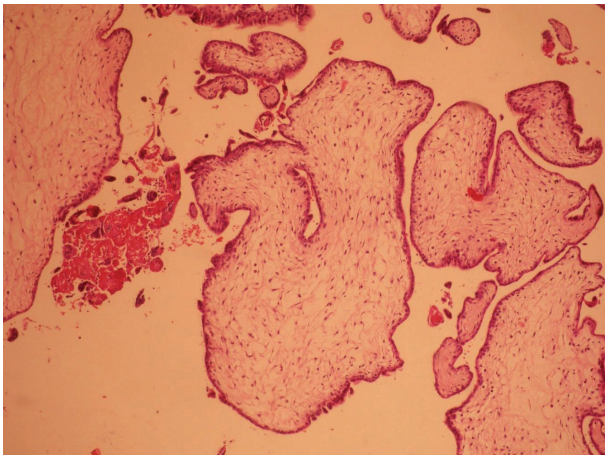

Image 2: Partial HM, large scalloped contoured villi with trophoblasts with paved invaginations and one inclusion. 10X H&E.

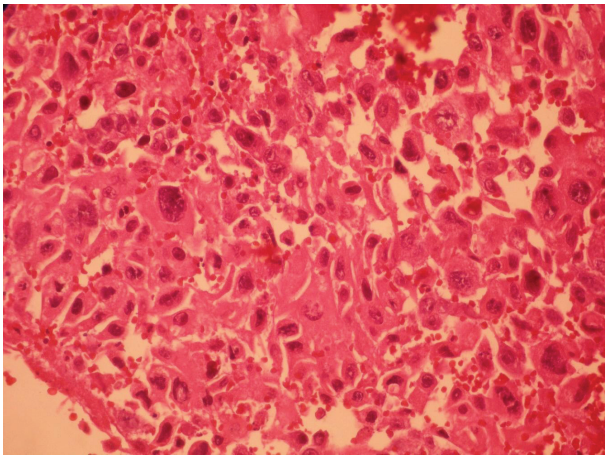

Image 4: Prominent trophoblastic atypical histology in complete hydatidiform mole. 40X H&E.

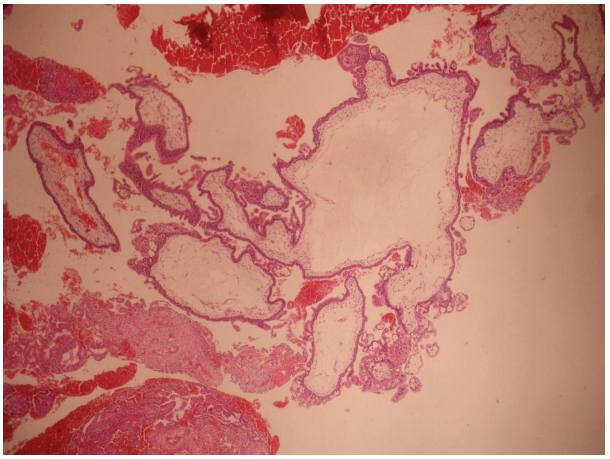

Image 3: Complete HM, completely large, cavitation and circumferential trophoblastic hyperplasia of villi consisting of lesions. 10X H&E.

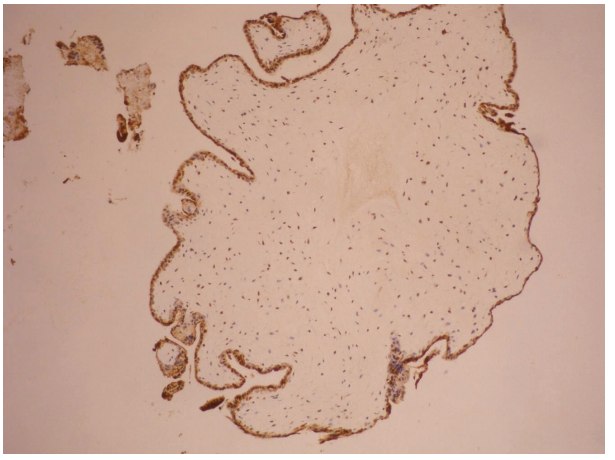

Image 5: Widespread and strong nuclear staining with p57KIP-2 is observed in trophoblasts in the villus containing a small cavitation with a large scalloped contour in the partial hydatidiform mole. 10X p57KIP-2.

(minimum: maximum) values. Categorical variables are expressed with n (%). The unpaired t-test was used in the comparison of age between HM groups. The Pearson chi-square test was used for comparisons of categorical variables among groups. Independent risk factors considered to be effective in HM detection were analyzed with binary logistic regression analysis. SPSS (IBM Corp. Released 2012. IBM SPSS Statistics for Windows, Version 21.0. Armonk, NY: IBM Corp.) The program was used for statistical analysis and $p<0.05$ was accepted as statistically significant.

RESULTS

The arithmetic mean age of the 907 pregnant women who underwent curettage due to abortion or termination of pregnancy was 29.64 (ranging between 13-54).

HM was diagnosed in 78 of 907 pregnant women (8.59%) who underwent curettage due to abortion or termination of pregnancy. 768 of these 907 pregnant women were Turkish (84.67%) and 139 of them were Syrian immigrants (15.33%) (Table 1). HM was diagnosed in 56 of 768 Turkish pregnant women (7.30%) and in 22 of 139 Syrian immigrant pregnant women (15.80%). There was a significant difference between Turkish women and Syrian immigrant women in terms of HM incidence (p=0.001).

Between the years 2016-2018, 33,108 live births took place in our hospital. 25,764 of these (77.82%) were Turkish and 7, 344 were Syrian (22.18%). HM was diagnosed in curettage of 56 Turkish women out of 768 and in 22 Syrian women out of 139. According to this result, the total HM incidence between the years 2016-2018 among all pregnant women was 2.29 per thousand (78/34 015), HM incidence in Turkish pregnant women was 2.11 per thousand (56/26 532) and in Syrian pregnant women it was 2.93 per thousand (22/7 483) and the difference between groups was not statistically significant (p=0.185).

While the arithmetic mean age of the 768 Turkish pregnant women was 30.41±6.83, the arithmetic mean age of 139 Syrian immigrant pregnant women was 25.40±7.22. The arithmetic mean age of the HM diagnosed 78 pregnant women was calculated as 27.94±8.07 (Table 1). HM frequency was higher in the group with age less than 20 compared to the group with age 35-39 (Figure 1). The arithmetic mean age of the HM diagnosed 56 Turkish pregnant women was 29.61±7.87 and the arithmetic mean age of the HM diagnosed 22 Syrian immigrant pregnant women was 23.18±6.71. The rate of Syrian pregnant women in the group aged younger than 20 was significantly higher (p<0.001). Similarly, the rate of Syrian pregnant women was also high in the group aged 20-24 (p=0.001). There was no significant difference in the group aged 25-29 (p=0.399). The rate of Turkish pregnant women was high in the group aged 30-34 (p<0.001). The rate for Turkish women was also high in the group aged 35-39 (p=0.032). The rate for Turkish women was also high in the group aged ≥40 years (p=0.035). The age dis-

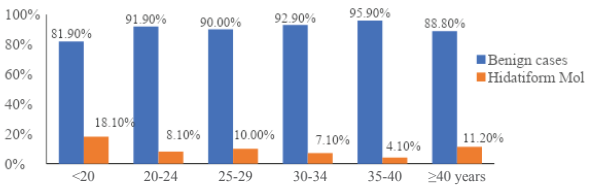

Figure 1: Age distribution of hydatidiform mole cases.

Table 1: Comparisons between hydatidiform mole and benign groups.

	Benign cases (n=829)	Hydatidiform mole (n=78)	p-value
Nationality			
Turkish	712 (92.70%)	56 (7.30%)	**0.001**[a]
Syrian	117 (84.20%)	22 (15.80%)	
Age	29.81±7.01 (13:54)	27.94±8.07 (14:47)	**0.017**[b]
Age group			
<20 years	59 (81.90%)	13 (18.10%)	**0.013**[a]
20-24 years	158 (91.90%)	14 (8.10%)	
25-29 years	181 (90%)	20 (10%)	
30-34 years	197 (92.90%)	15 (7.10%)	
35-39 years	163 (95.90%)	7 (4.10%)	
≥40 years	71 (88.80%)	9 (11.30%)	

Data is given as n (%) and mean ± standard deviation (minimum: maximum).
a: Pearson chi-square test, b: Independent samples t test.
Percentages given in the table are reported according to the variables in the rows.

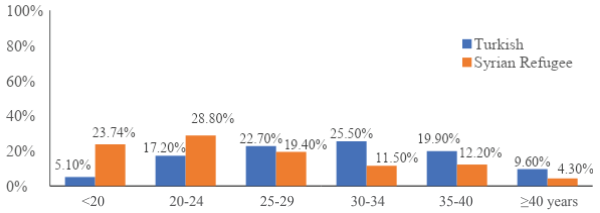

Figure 2: Age distribution of Turkish and Syrian immigrant pregnant women who underwent curettage.

tribution of Turkish and Syrian immigrant pregnant women who underwent curettage is shown in Figure 2.

Risk factors affecting HM occurrence is shown in Table 2. Nationality was found to be a risk factor in HM determination and the risk was 2.06 times higher in Syrian than Turkish women. Presence in the group aged 35-39 years was detected as a protective factor with respect to the group aged <20 years. Presence in the group aged 35-39 years reduced the risk of HM detection at a rate of 74%.

Table 2: Risk factors affecting hydatidiform mole occurrence.

Risk Factor	Wald	OR (95%CI)	p-value
Age Group			
<20 (Ref. Cat)	-	-	-
20-24	3.14	0.47 (0.21:1.08)	0.076
25-29	1.20	0.64 (0.29:1.42)	0.274
30-34	3.15	0.47 (0.20:1.08)	0.076
35-39	7.16	0.26 (0.10:0.70)	**0.007**
≥40	0.26	0.78 (0.30:2.03)	0.609
Nationality			
Turkish (Ref. Cat.)	-	-	-
Syrian	6.14	2.06 (1.16:3.64)	**0.013**

Logistics regression model was significant (p=0.004)
OR: Odds ratio, CI: Confidence interval, Ref. Cat: Reference category

DISCUSSION

At the end of this study, the incidence of HM in curettage materials performed due to abortion or termination of pregnancy in 768 Turkish pregnant women was 7.30%. This value is in conformity with previous studies performed in Turkey. The incidence of HM in curettage materials performed due to abortion or termination of pregnancy in 139 immigrant pregnant women was 15.80%. Statistically, the HM incidence in Syrian immigrant pregnant women was significantly higher (2.06 times) than Turkish women. The arithmetic mean age of Syrian pregnant women was lower than that of Turkish pregnant women. Age and nationality were detected as risk factors for HM.

In the literature, the incidence of HM is usually given over the number of pregnancies, but the incidence in curettage materials due to abortion or termination of pregnancy has been analyzed less. We could find only three research studies in the literature that examined HM incidence in curettage materials due to abortion or termination of pregnancy. Biscaro et al. found the HM incidence in Brazilian pregnant women who underwent curettage due to abortion or termination of pregnancy to be 2.24% (10 HM in 446 curettage materials) (12). In our study, the incidence of HM in Turkish pregnant women in our country who underwent curettage due to abortion or termination of pregnancy was 3.3 times higher than Brazilian women. However, in Germany, in the study performed by Horn et al. (27), the incidence of HM in curettage materials due to abortion or termination of pregnancy in German pregnant women was 5.1%. In the study performed by Mulisya et al. in Uganda (25), the incidence of HM in Ugandan (sub-Saharan Africa) pregnant women was 6.1% (11 HM in 118 curettage materials) and in the study performed by Adalı et al. in Turkey (3), the incidence of HM in Turkish pregnant women in the Kars province was 6.9% (19 HM in 277 curettage materials).

The aim of this study was to compare the HM incidence in curettage materials due to abortion or termination of pregnancy in Syrian immigrant pregnant women and Turkish pregnant women. At the end of the study, it was found that the incidence of HM in curettage materials due to abortion or termination of pregnancy in Syrian immigrant pregnant women was significantly higher than Turkish pregnant women. The fact that pregnancy in adolescence is approximately 5 times higher in Syrian immigrant women explains the high HM incidence. Besides this, stress (war and migration), low socio-economic level and probable infections that may occur due to these factors may have contributed to this increase in HM incidence. The effect of these variables on the incidence of HM in immigrants should be analyzed in future studies.

The likelihood of many more induced abortions in Turkish pregnant women should not be overlooked during the assessment of the data. Despite the fact that both societies are Muslim, induced termination of pregnancy in curettages under 10 weeks may cause a decrease in the HM rate in Turkish pregnant women.

An important limitation of the study is that this was a mono-centre study. What is the situation in other hospitals in the province of Bursa? What is the situation in private hospitals? Further research studies are necessary on these issues. Another limitation is that this was a retrospective study. For this reason, probable causes that may affect HM could not be interrogated.

In conclusion, this is the first study that investigated the incidence of HM in Syrian immigrant pregnant women. In our

region, the incidence of HM in Syrian immigrant pregnant women was significantly higher than Turkish pregnant women. Major probable causes that may affect HM incidence in Syrian immigrant pregnant women are nationality and age. The effect of factors such as socio-economic level, nutrition, infection, stress and exposure to conditions of warfare on this situation should be analyzed in further studies.

Ethics Committee Approval: Bursa Higher Specialization Training and Research Hospital, Clinic Researches Ethical Committee Number: 2011-KAEK-25 2018/11-25.

Informed Consent: Written consent was obtained from the participants.

Peer Review: Externally peer-reviewed.

Author Contributions: Conception/Design of Study- T.E., H.D..; Drafting Manuscript- T.E., H.D..; Final Approval and Accountability- T.E., H.D.

Conflict of Interest: Authors declared no conflict of interest.

Financial Disclosure: Authors declared no financial support.

Etik Komite Onayı: Bursa Yüksek İhtisas Eğitim ve Araştırma Hastanesi Klinik Araştırmalar Etik Kurulu Numara: 2011-KAEK-25 2018/11-25.

Bilgilendirilmiş Onam: Katılımcılardan bilgilendirilmiş onam alınmıştır.

Hakem Değerlendirmesi: Dış bağımsız.

Yazar Katkıları: Çalışma Konsepti/Tasarım- T.E., H.D.; Yazı Taslağı- T.E., H.D..; Son Onay ve Sorumluluk- T.E., H.D.

Çıkar Çatışması: Yazarlar çıkar çatışması beyan etmemişlerdir.

Finansal Destek: Yazarlar finansal destek beyan etmemişlerdir.

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