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In Southern India, the Prevalence of Diabetes Mellitus and Cervical Malignancy among Girls and Women

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Abstract

Introduction: In women all around the world, cervical carcinoma is the second most prevalent type of cancer that they will face.

. It is estimated that there are around 365.71 million women in India who are over the age of 15 and are having an elevated risk of acquiring cervical cancer. Herpes, oral contraceptives, and immunodeficiency diseases are all examples of risk factors. Other risk factors include smoking. It has been demonstrated in the scientific literature that There is a correlation between having type 2 diabetes mellitus (T2DM) and an increased likelihood of developing various cancers, including endometrial, pancreatic, and hepatic tumours. This study was carried out with the purpose of discovering whether or not there is a relationship between the phenomenon being investigateddiabetes mellitus and cervical cancer in females.

The Components and Procedures: Individuals who have been diagnosed with cervical cancer, regardless of whether or not they had diabetes, were separated into two distinct groups according to those patients' menopausal state. The version 11.5 of SPSS was applied for the purpose of data analysis. Calculations were made for the chi-square test as well as odds ratios. When it comes to P-values, the threshold for statistical significance was established at 0.05 degrees.

Results: According to the findings, there were 29% of patients diagnosed with cervical cancer who were between the ages of sixty and seventy, and the majority of these individuals (40%) were married and had many childrenDespite the fact that the Although the association between body mass index and the likelihood of developing cervical cancer in diabetic individuals was not found to be statistically significant in either the pre-menopausal or post-menopausal groups, type 2 diabetes in cervical carcinoma is a good indication of the likely outcome of the disease.This is the case even if the relationship was not significant.

Conclusions: The risk of developing cervical cancer is higher for women who have diabetes and have achieved menopause; hence, it is imperative that these women be obliged to undergo routine screening. To be able to generalize the findings, it will be essential to carry out more study conducted over a longer period of time.

***Keywords*:** cervicalcarcinoma,menopause, diabetes, body mass index, and metformin.

Introduction

The metabolic disorder known as diabetes mellitus can be attributed to a variety of different etiological factors. It is characterized by persistently high Blood sugar levels that are brought on by a malfunction in either the manufacturing of insulin or the action of insulin, or at the very least, both of these processes, are referred to as hyperglycaemia. A kind of diabetes mellitus, often known as type 1 diabetes mellitus, is

a condition that affects the body. (TIDM), is a disorder that manifests itself when the body is unable to create insulin that is active. Type 2 diabetes mellitus, often known as T2DM, is characterized by insulin resistance, which is the underlying cause of the condition. It has been proven that the risk is increased when there are mutations in the PPARγ gene, which is placed The ABCC8 and KCNJ11 genes, which are found on chromosome 11, as well as the CALPN 10 gene, which is found on chromosome 2, are all situated on chromosome 3. Nearly 5 million people had diabetes by the time the year 2015 arrived, making it the greatest cause of death in the world. The number of children in India who are afflicted by TIDM is the second most in the world, making India the second largest country in the world. Women all over the world are affected by cervical cancer, which is the second most frequent type of cancer that affects women. The second most prevalent type of cancer that is diagnosed in females is this particular type. This particular type of cancer is the sixth most common type of cancer found in human beings. The majority of cases of this particular form of cancer are found in females in India. and it has been established that this specific form of cancer is the most prevalent cause of mortality caused by cancer in nations that are considered to be developing. Over the age of 15, there are roughly 365.71 million women in India who are at an increased risk of acquiring cervical cancer. This population is considered to be at a greater risk. The use of oral contraceptives, immunodeficiency diseases, herpes, and smoking are all crucial aspects to take into mind because they are all possible risk factors. When compared to other kinds of cancer, cervical cancer typically manifests itself at a younger age than other types of cancer. With a median age of 38 years (range from 21 to 67 years), the incidence of cervical cancer begins to increase in the age group of 30–34 years and reaches its greatest point between the ages of 55–65 years. Furthermore, the median age of the disease is 38 years. A number of genes, including UBE2C, CCNB1, CCNB2, NIP210, MELK, and CDC20, among others, have been shown to have an abnormally high level of expression in malignancies, according to reports from research. Concerning the genetic link between diabetes mellitus and individuals who are afflicted with cancer of the cervix, the scientific community does not possess any evidence that can be deemed tangible in this regard. A consensus report prepared by experts from the American Diabetes Society and the American Cancer Society re-evaluated the association between malignancy incidence and diabetes, examining common risk factors, biochemical connections, and the relationship between diabetes treatment and cancer risk. It was found that type 2 diabetes may increase the risk of specific cancers, particularly hepatic, pancreatic, and endometrial cancers. This was the conclusion reached by the consensus report. On the other hand, there was no data that could be regarded definitive supporting the hypothesis that type 2 diabetes is linked to cervical cancer. In light of the fact that there were risk variables that were equivalent, it is not out of the question that this association was extended. There was a distinction made between reversible risk variables, which included diet, physical activity, alcohol intake, and smoking, and non-reversible risk factors, which included age and gender at the time of the study.

Inflammation, hyperglycaemia, and hyperinsulinemia with activation of the IGF-1 axis are all components of the molecular relationship that was shown to be associated with it. Exogenous insulin, on the other hand, may be related with a higher risk of cancer, but metformin may be associated with a decreased risk of cancer, according to research that was conducted in the past. In order to determine the prevalence of cervical cancer in patients with type 2 diabetes and the risk of getting the disease, the Epidemiological Department of Mexico conducted a population-based study that was cross-sectional in nature. The goal of the investigation was to determine the risk of developing the disease. In a study involving 160 cases of cervical carcinoma and 25,262 controls, researchers concluded that the prevalence of cervical carcinoma in females with type 2 diabetes is significantly elevated compared to those without diabetes (1,336 cases per 100,000 inhabitants versus 576 cases per 100,000 inhabitants, $p < 0.001$). This conclusion was derived from the observation that the incidence of cervical cancer in women with diabetes is markedly elevated compared to that in women without diabetes.

The LKB1-AMPK-mTOR signalling pathway is posited to be implicated in protein production within cervical cancer cells of diabetes individuals. This theory was based on the findings of the study. This

system is in charge of monitoring and responding to a variety of elements that regulate protein synthesis, including the availability of nutrients, the efficiency of energy use, stress, hormones, and mitogens. The fact that this cascade plays a crucial role This research demonstrates the evolution of cancer and diabetes. The examination investigating the correlation between metformin consumption and the incidence of cervical cancer involved research on persons diagnosed with type 2 diabetes. This study was among the initial cohort studies to indicate that metformin usage may reduce the incidence of cervical cancer compared to individuals using other hypoglycaemic medications. The study was conducted by National Taiwan University of Medicine. This observation was hypothesized to result from the anti-inflammatory properties of Metformin or the inhibition of pro-inflammatory pathways, including the nuclear factor-κB and signal transducer and activator of transcription 3 (STAT3) pathways. Moreover, it has been found that metformin suppresses the proliferation of malignant cervical cells by activating AMPK in an enzyme-independent way. This inhibits the proliferation of malignant cells in the cervix.

The prognostic The relationship between diabetes and the prognosis of cervical cancer was examined by a meta-analysis and a comprehensive review, respectively. Eleven separate pieces of research were used into the meta-analysis. The findings of the study suggested that individuals with type 2 diabetes had a poor overall survival rate as well as a low recurrence-free survival rate. The study investigated a total of 11,091 patients, and the findings indicated that the patients had a low survival rate overall. It is clear from this that the presence of type 2 diabetes is a key factor in predicting the prognosis of individuals who have been diagnosed with colorectal cancer. Based on the results of the subgroup analysis, it was shown that diabetes had a distinct connection with a lower overall survival rate. Type 2 diabetes is an indication that is best suited for assessing the prognosis of cervical cancer. This is because the diagnosis of type 2 diabetes is rather straightforward.

MATERIAL AND METHODS

Research on hospital-based case control was carried out at hospitals for the current investigationsthat are connected with Meenakshi Medical College Kanchipuram, which is situated in the state of Tamilnadu in India. The research was carried out over the period of roughly three months. The census that was conducted out in the year 2001 revealed that the city has a high literacy rate of around 82.2%, which includes a high female literacy rate as well. This information was obtained from the census. This suggests that the city is in possession of an exceptional literacy rate. The initiative, which has been authorized by the Institutional Ethics Committee in the past, was given their permission once again. Women who had been diagnosed with cancer of the cervix (using the usual techniques) and who had been admitted to the study hospital throughout the time period of the study were taken into consideration throughout the course of the research. Through the utilization of the techniques that are generally accepted, a diagnosis of diabetes was either established or confirmed. In all, there were sixty cases and sixty controls, which led to a total sample size of one hundred twenty. This was the outcome of the total number of cases and controls. Our method of sampling, which is known as convenience sampling, was utilized up to the point when the sample size was attained.

We went through the process of developing, validating, and utilizing a questionnaire that had a systematic framework. A number of themes were discussed, one of which being the subject's awareness of cancer and diabetic disorders. It was determined that information concerning the socio-demographic features of the participants may be acquired. The research did not include patients who were hesitant to take part in the study because they were excluded from research. In this study, patients who were diagnosed with cervical cancer and either had diabetes or did not have diabetes were separated into two groups based on whether or not they had reached menopause. The participants in these groups were women who were at least sixty years old, had not experienced menstruation without the use of medication for a period of more than one year, and had levels of follicle stimulating hormone and estradiol that were within the range of what is considered to be post-menopausal or equivalent.

It was decided to use SPSS version 11.5 in order to conduct the analysis of the data. Through the utilization of the proper tables and graphs, the data were presented in the form of proportions. The c2 test was applied in addition to the calculations that were performed in order to establish odds ratios. The

p-values that were considered to be statistically significant were those that were either lower than or equal to 0.05. Table 1 of the data reveals that There was a median age of 57.50 years old among the patients who were included in both the cases and the controls. This data is incorporated into the table that is provided. All of the patients had been diagnosed with cervical cancer for at least two years previous to the completion of the surgery. The majority of the patients had been diagnosed with the disease. On the other hand, blood group A was the most prevalent among the individuals who served as controls, and blood group O was the most prevalent among the individuals of the patients. Fourty percent of the women had a high parity score that was higher than P3L3, with P4L4 being the most common score and P10L9 being the highest conceivable score. This was the case in all of the situations. It was found that the severity of the disease was greater than stage IIb in the majority of instances, with stage IIIb being the stage that occurred the most frequently overall. The histological form that was shown to be the most prevalent was referred to as large cell non-keratinizing squamous cell carcinoma (LCNKSCC)which accounted for 36 percent of all cases. Squamous cell carcinoma with moderate differentiation (MDSCC) came next, accounting for 27 percent of all cases. This was the second most common kind of squamous cell carcinoma.

Metformin was used to treat the majority of diabetes patients in both the case group and the control group. Insulin therapy was then delivered once the metformin treatment was completed. a cancerous growth of the thyroid In Figure 1, we show the association between diabetes and cervical cancer in postmenopausal women who have the condition, as well as in patients who do not have cervical cancer. This correlation is similar in patients who do not have cervical cancer. Statistically speaking, the fact that the p-value is 0.0014, which is the value, is evidence of significance. a cancerous growth of the thyroid Figure 2 depicts the link between diabetes and cervical cancer in women who have not yet reached menopause. In addition, individuals who do not have cervical cancer are included in this research comparison. It was determined that the findings did not satisfy the requirements for statistical significance. Patients with cervical cancer who were either pre-menopausal or post-menopausal were subjected to a univariate analysis in order to locate the factors that were associated with an increased likelihood of developing diabetes mellitus. Table 2 displays the findings of this research study for your perusal. It was determined that the risk variables that were taken into consideration were high blood pressure, an increased body mass index (BMI), and anemia. There was not a single one of the aforementioned findings that could be considered statistically significant. The comparison of the case group with the control group is presented in Table 3, which also includes the co-morbidities. On the other hand, the majority of the controls were diagnosed with different forms of cancer, whereas the majority of the cases were diagnosed with respiratory diseases.

Discussion

Within the population of females residing in Kanchipuram, the research was conducted to analyze the data to establish whether or not there was a connection between diabetes and the likelihood of developing cervical cancer. "Thestudy was conducted on sixty people who had been diagnosed with cervical cancer as well as sixty persons who served as controls and were of the same age. With a standard deviation of 11.3, the average age of both the cases and the controls was 56.50 years, with cases being older than controls. It was found that 29% of the patients were between the ages of sixty and seventy, which shows that people in this age group are at a possible risk of acquiring cancer of the cervix, which is frequent in India. This information was uncovered by the researchers. The results of West's study, which were published in the British Journal of Cancer, are in agreement with this statement.

The findings of yet another research that White and his colleagues conducted indicate that the chance of acquiring cervical cancer does not begin to reduce until the age of 85. This assertion is supported by the outcomes of the study. In addition to this was the conclusion that was reached over the course of the investigation. As a consequence of this, screening need to be carried out between the ages of 21 and 85. Our investigation revealed that around forty percent of the women who were diagnosed with cervical cancer were also multiparous. This was one of the findings that we discovered. A great number of investigations have come to the same conclusion, which is consistent with this. It was Eluf-Neto and his colleagues who were the ones who originally reported it in the year 1994. This means that women

who have had at least five children have a relative risk of acquiring cancer of the cervix that falls somewhere in the range of 3.8 to 4.4 of developing the disease.

According to the findings of another study that was carried out in Finland, the bulk of the rise in the incidence of cervical cancer among multiparous women was noticed among women who were under the age of fifty. Both the age at which the first child was born and the amount of time that had elapsed after the previous birth were additional factors that were taken into consideration. A possible explanation for this result is that the accelerated metaplastic response of squamous epithelial cells that takes place during pregnancy is the cause of this phenomenon. Because of this response, the cervical epithelium becomes more prone to undergoing a change into a cancerous state.

Our investigation also revealed that poorly differentiated LCNKSCC/SCC is the most prevalent histological subtype among patients, accounting for 36 percent of all cases. This was the most frequent subtype among cases. This is next followed by SCC that is substantially differentiated, which accounts for 27 percent of all instances. It has been documented by Kuo et al. that SCC is a common occurrence in diabetic persons. This discovery is consistent with the data that we have obtained from our own research.

An increase in the expression of IGF-1R has been linked to a variety of cancer types, such as breast, liver, and cervical cancer, as per the results of a study conducted by Kuo and colleagues. The development of cervical cancer is influenced by a combination of genetic factors and environmental factors, including infection with the human papillomavirus. The illness is the result of this interaction. The metaplastic area of the squamous-columnar junction is the region of the junction that is affected, as per the human papillomavirus. It is located between the endocervix and the cervix and the ecto-cervix, which is the junction in question. This metaplastic syndrome may have been brought on by the constant inflammation that is brought on by diabetes mellitus, which is one of the probable causes. In addition, the research that was described before provides evidence that HLA class II haplotypes have a role in the progression of cancer that affects the cervix. Additionally, diabetes may have an influence on these genes. This is as an extra option. As a result of this, diabetes has an effect on environmental variables as well as hereditary factors, both of which are factors that lead to the development of cervical cancer syndrome.

A similar distribution was found between the case group and the control group in terms of the average weight and body mass index (BMI) of 116 patients, as assessed by our research. To be more specific, the weight of sixty cases is 50.05 ±11 kg, and the body mass index (BMI) is 22.15 ±5. According to this perspective, the outcomes of the inquiry that was carried out by other researchers [11] are compatible with this explanation. The results of our study suggested that the body mass index (BMI) was not a significant risk factor for cervical cancer among diabetics in pre-menopausal and post-menopausal age groups. This was demonstrated by the univariate analysis, which produced a null hypothesis ($p = 0.27719$). In accordance with the findings of a research that was carried out in 2016 by Jiamset and colleagues, who reached the same conclusions ($p = 0.278$), this is in agreement with the findings. In addition, the research that was discussed earlier highlighted the fact that there was a significant correlation between type 2 diabetes and the absence of relapse for a period of five years, in addition to the existence of cervical cancer in general ($p = 0.008$) [25]. When it comes to cervical cancer, the presence of type 2 diabetes is a beneficial predictive factor, since other study has discovered results that are comparable to the findings that were described before. The purpose of the univariate analysis that we carried out as part of our research was to determine whether or not hypertension and anemia were independently linked with the development of diabetes in individuals who had been diagnosed with cervical cancer.

With a p-value of 0.2187735, the two links that were mentioned before did not satisfy the requirements for statistical significance or fit the criteria. Despite the fact that these linkages do exist, they have not been taken into consideration in any of the previous study. The research offers a number of benefits, one of the most significant of which is that it takes into consideration both hypertension and anemia as possible risk factors. Additionally, it contains an equal number of cases and controls that are of the same age. There have been previous studies that have studied the relationship between diabetes and a variety of cancers, including breast, liver, and

uterine cancer; however, the connection between diabetes and cervical cancer is a discovery that has only been made relatively recently. A small sample size and a lack of information regarding lifestyle factors such as physical activity, nicotine usage, alcohol use, and lifestyle choices are two of the limitations of this study. Nevertheless, this study does have some limitations regarding lifestyle factors. The existence of co-morbidities that were connected with the ages of the patients was another factor that contributed to the confusion that was present.

CONCLUSIONS

Within the community of women who have attained menopause, this article throws light on a v people are aware that cervical cancer is one of the leading causes of death among women, and it is also common knowledge that India is a centre for diabetes across the world. Countries that are considered to be undeveloped are responsible for more than a quarter of the worldwide burden of cervical cancer. As a result, women who have attained menopause and have diabetes have an increased likelihood of developing cervical cancer over time. As a consequence of this, they ought to be examined on a consistent basis in order to detect the problem at an earlier stage, receive treatment, and have a greater chance of surviving. Additional research that is carried out over a more extended length of time is necessary in order to determine whether or not the findings may be generalized. One of the disadvantages of this study is that it was carried out for a relatively short amount of time and on a relatively small sample size. Both of these factors contribute to the limits of the study.

Table1.Demographicdetailsofpatients(*N*=60)

Indicator	**Cases, (%)**	***n*Controls,*n*(%)**	**Total, *N* (%)**
Age(years)			
30–40	3(5.99)	3(5.99)	8(5.99)
40–50	11(16.66)	11(16.66)	20(16.66)
50–60	20(35)	20(35)	42(35)
60–70	18(28.33)	18(28.33)	34(28.33)
70–80	8(13.33)	8(13.33)	16(13.33)
Height[cm]	150.57±7	152.07±6	
Weight[kg]	50.05±11	49.66±9	
Bodymassindex[kg/m^2]	22.15 ±5	21.44±3	
Durationof illness (years)			
<1	1(1.67)		
1–2	3(5)		
2–3	17(28.33)		
3–4	8(13.33)		
4–5	15(25)		
5–6	6(10)		
>6	10(16.66)		
Bloodgroup			
O+	38.3(23)	8(13.33)	
O–	1(1.7)		
A+	16(26.7)	11(18.3)	
A–	1(1.7)		
B+	15(25)	8(13.33)	
B–	3(5)		

Table -2 Cases–patients with carcinoma cervix and diabetes mellitus, controls–patients without carcinoma cervix, with diabetes mellitus

Risk factor	**Cases, *n*(%)**	**Controls,*n*(%)**	**Odds ratio**	***p*-value**
Hypertension (in post- menopausal women)				0.218(NS)
Absent	10(40)	7(70)	3.5	
Present	15(60)	3(30)		
Hypertension (in pre-menopausal women)				
Absent	3(60)	7(70)	0	0.5460(not significant)
Present	2(40)	3(30)		
Body mass index (in post-menopausal women)				
Elevated	14(56)	2(20)	5.09	0.1197(not significant)
Normal	11(44)	8(80)		
Body mass index (in pre-menopausal women)				

Elevated	4(80)	0	0	0.2771(not significant)
Normal	1(20)	2(100)		
Anemia (in post-menopausal women)				
Absent	7(28)	4(40)	1.714	0.7735(not significant)
Present	18(72)	6(60)		
Anemia (in pre-menopausal women)				
Absent	3(60)	1(50)	1.5	0.8091(not significant)
Present	2(40)	1(50)		

Table3.Co-morbiditiesincasesandcontrols

Co-morbidities	Cases,*n*(%) *N*=60	Controls,*n*(%) *N*=60
Dataunavailable	48(80)	3(5)
Respiratorysystem	1(1.7)	6(10.2)
Cardiovascularsystem	1(1.7)	1(1.7)
Gastro-intestinalsystem	1(1.7)	1(1.7)
Genito-urinarysystem	3(5.1)	2(3.8)
Centralnervoussystem	1(1.7)	1(1.7)
Othercancers		
Breast	1(1.7)	14(23.8)
Gastrointestinalsystem	1(1.7)	12(20.4)
Lung	1(1.7)	2(3.8)
Ovary		4(3.8)
Tonsil		2(3.8)
Others	5(8.5)	11(18.7)

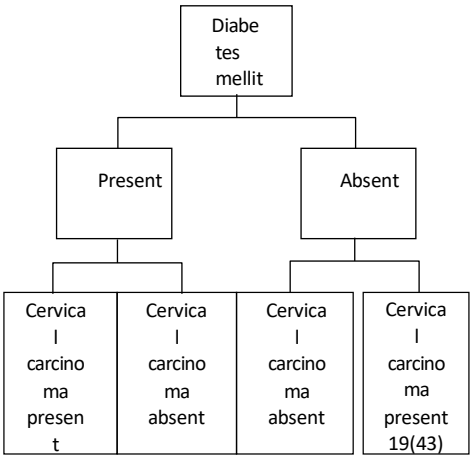

Fig.1.Associationofdiabetesinpost-menopausalwomen

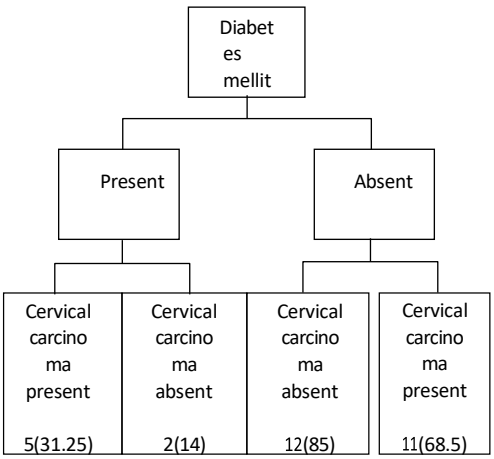

Fig. 2. Associationofdiabetesinpre-menopausalwomenwith and without cervical carcinomacervicalcarcinoma

REFERENCES

1. World Health Organization. Diabetes Programme: About Diabetes. Available from: http://www.who.int/diabetes/action_online/basics/en/.
2. Maori L, Ezekiel D, Bilal J. Prevalence of diabetes in Zambuk General Hospital. Rep Opinion 2012; 4: 54-57.
3. Largay J. Case study: new-onset diabetes: how to tell the difference between type 1 and type 2 diabetes. Clin Diabetes 2012; 30: 25-26.
4. David M , Mayer B, Davidson RA, Defronzo RJ, Heine RR. Impaired fasting glucose and impaired glucose tolerance. Diabetes Care 2007; 30: 753-757.
5. World Health Organization. Genetics and diabetes. Available from: http://www.who.int/enomics/about/Diabetis-fin.pdf.
6. Cavan D, Fernandes J, Makaroff L, Ogurtsova K, Webber S. IDF Diabetes atlas (7th ed.). International Diabetes Federation 2015.
7. WHO/ICO Information Centre on HPV and Cervical Cancer (HPV Information Centre). Summary report on HPV and cervical cancer statistics in India 2007. Available from:http://www.who.int/hpvcentre.
8. Schiffman M, Castle PE, Jeronim J, Rodrigue AC, Wacholde S. Human papillomavirus and cervicalcancer. Lancet 2007; 370: 890-907.
9. Singh N. HPV and cervical cancer – prospects for prevention through vaccination. Indian J Med Paediatr Oncol 2005; 26: 20-23.
10. Giovannucci EHDM, Archer MC, Bergenstal RM, et al. Diabetes and cancer. Diabetes Care 2010; 33: 1674-1685.
11. López-Hernández D. Type 2 diabetes mellitus and habits lifestyle increases the risk of cervical cancer: a cross-sectional population – based study. Austin J ObstetGynecol 2014; 1: 1-7.
12. Chen S, Tao M, Zhao L, Zhang X. The association between diabetes/hyperglycemia and the prognosis of cervical cancer patients: a systematic review and meta-analysis. Medicine 2017; 96: e7981.
13. Tseng CH. Metformin use and cervical cancer risk in female patients with type 2 diabetes. Oncotarget 2016; 7: 59548.
14. West RR. Cervical cancer: age at registration and age at death. Br J Cancer 1977; 35: 236-241.