Original Article

Relation of Wilms Tumsor 1 scores with the Age of Ovarian Carcinoma Patients

DOI: dx.doi.org

Md Zahid Hossain[1*], Mahmuda Naznin[2], Saifeen Parvin[3], Alimul Hasan[4], Md Fakhrul Hassan[5]

Received: 14 January 2024
Accepted: 27 January 2024
Published: 10 February 2024

Published by:
Sher-E-Bangla Medical College, Barishal, Bangladesh

*Corresponding Author

Editor: Prof. Dr. HN Sarker

Available Online:
https://bdjournals.org/index.php/planet/article/view/422

ABSTRACT

Introduction: *Worldwide, ovarian carcinoma is the seventh most common cancer and the eighth leading cause of death among women. Several studies reported Wilms tumor 1 (WT1) score as a potential marker for differentiating ovarian serous carcinoma from endometrial serous carcinoma.* ***Aim of the study:*** *This study aimed to assess the relation of Wilms tumor 1 score with the age of ovarian carcinoma patients.* ***Methods and materials:*** *Between July 2019 and June 2021, a cross-sectional descriptive study occurred at two notable medical institutions in Bangladesh: Rajshahi Medical College Hospital (RMCH) in Rajshahi and Bangabandhu Sheikh Mujib Medical University (BSMMU) in Dhaka. The study encompassed 31 suspected ovarian carcinoma cases admitted to RMCH, later confirmed through histopathological analysis. Participants were selected using purposive sampling, and data analysis utilized Microsoft Excel and SPSS version 20.0.* ***Results:*** *In assessing the relation between WT1 scores and the age of the subject we observed that age groups of 51-60 years showed the maximum positive staining. Among 66.6% of them showed >50% (3+), 11.1% of them showed 11-50% (2+) and 11.1% of them showed 1-10% (1+) WT1 scores. Only 11.1% of them showed negative.*

(The Planet 2023; 7(1): 199-207)

1. *Pathologist, Department of Pathology, Rajshahi Medical College, Rajshahi, Bangladesh*
2. *Assistant Professor, Department of Microbiology, Rajshahi Medical College, Rajshahi, Bangladesh*
3. *Assistant Professor, Department of Pathology, Diabetic Association Medical College, Faridpur, Bangladesh*
4. *Clinical Pathologist, Rangpur Medical College Hospital, Rangpur, Bangladesh*
5. *Lecturer, Department of Pathology, Kushtia Medical College, Kushtia, Bangladesh*

The age group of 20-30 years showed the maximum negative staining. Only 16.6% of them showed WT1 scores 11-50% (2+). We did not find any significant relation between WT1 and age. (P=0.220. ***Conclusion:*** *There is not any significant relation between Wilms tumor 1 scores and age of ovarian carcinoma patients.*

Keywords: *Wilms tumor score, WT1 scores, Ovarian carcinoma, Serous, Endometrioid*

INTRODUCTION

The ovaries are paired, egg-shaped structures that share homology with the testes, albeit being smaller in size. Throughout the reproductive years, the average dimensions of ovaries are typically around 4×2×1 cm [1]. Affixed to the upper pole of the ovary, one can find the ovarian fimbria and suspensory ligament [2]. Ovarian cancer ranks as a highly fatal gynecological malignancy in women, holding the unfortunate distinction of being a leading cause of death among gynecological cancers [3,4]. Incidence rates of ovarian cancer are notably elevated in Europe and Northern America, while the lowest rates are observed in Africa and Asia [5]. Ovarian carcinoma stands out among gynecological cancers due to its remarkable aggressiveness, coupled with a mortality rate that surpasses its incidence rate [6,7]. Typically, the diagnosis of ovarian cancer occurs during advanced stages (II-IV), characterized by invasive growth extending beyond the ovarian surface, and dissemination throughout the peritoneal cavity and pelvis [8]. Of the ovarian carcinoma subtypes, epithelial ovarian carcinoma is the most prevalent, accounting for around 60%-70% of all cases [9]. Research has revealed that ovarian carcinogenesis originates from the ovarian surface epithelium, with subsequent metaplastic changes giving rise to distinct cell types. Originally identified as a tumor suppressor gene located on chromosome 11p13, the Wilms tumor gene (WT1) displays a unique expression pattern. Unlike many other tumor suppressor genes, WT1's expression within normal human tissue is primarily confined to the urogenital system and mesoderm-derived tissue [10]. Notably, positive WT1 staining is observable in normal tissues like the fallopian tube, kidney, mesothelium, ovarian granulosa cells, Sertoli cells, and spleen [11]. Among the limited spectrum of carcinomas exhibiting nuclear WT1 expression, ovarian and fallopian tube carcinomas have been reported to do so [12]. This expression pattern aligns distinctly with serous phenotypes, with considerably lower staining observed in other morphological subtypes of ovarian carcinoma [13]. The Wilms tumor gene, WT1, encodes a protein featuring four zinc fingers, and it has been recognized for its role in transcriptional regulation, influencing genes encompassing growth factors, differentiation markers, cell-cycle regulators, and apoptosis regulators. However, recent discoveries have illuminated WT1's dual role as both a participant in transcriptional regulation and an oncogene in ovarian tumors. Extensive research has delved into WT1 expression within ovarian cancers, with a pronounced positive expression evident in serous adenocarcinomas. This notable expression is particularly prevalent in serous carcinoma, which sets it apart from other subtypes due to its aggressive behavior and distinctive genetic alterations

[4]. The objective of this current study was to assess the relation of Wilms tumor 1 score with the age of ovarian carcinoma patients.

METHODS & MATERIALS

Conducted between July 2019 and June 2021, this cross-sectional descriptive study was carried out jointly by the Department of Pathology at Rajshahi Medical College Hospital (RMCH) and the Department of Pathology at Bangabandhu Sheikh Mujib Medical University (BSMMU) in Dhaka, Bangladesh. The study focused on 31 cases of clinically suspected ovarian carcinoma, which were initially admitted to Rajshahi Medical College Hospital (RMCH) and subsequently confirmed as ovarian carcinoma through histopathological examination. These 31 cases constituted the study subjects and were selected using a purposive sampling technique. The study was ethically approved by the respective hospital's ethical committee, and informed consent was duly obtained from all participants before data collection. The study's exclusion criteria involved the removal of patients who were clinically suspected but not histopathologically confirmed as having ovarian carcinoma. Detailed demographic and clinical information for each participant was meticulously recorded. To process, analyze, and present the collected data, Microsoft Excel and SPSS version 20.0 were utilized as required tools. In terms of statistical analysis, a significance level was set at $P < 0.05$ to determine the presence of significance.

RESULT

In the present study, when examining the age distribution of the entire patient cohort, it was determined that the age range spanned from 20 to 75 years. The cases were further categorized into groups based on decades. Notably, the highest proportion (29.0%) of patients fell within the age group of 51 to 60 years. Following closely, the subsequent most common age group was 31 to 40 years, accounting for 25.8% of cases. The median age for the patients was calculated as 47.0 years, while the mean age ± standard deviation (SD) of the participants was found to be 45.10 ± 13.78 years (**Table I)**.

Table I: Distribution of participants as per age (N=31)

Age (Year)	n	%
20-30	6	19.4
31-40	8	25.8
41-50	5	16.1
51-60	9	29
>61	3	9.7

Upon analyzing the histologic subtypes within the group of 31 cases, it was evident that serous subtypes exhibited the highest frequency, accounting for a total of 16 cases (51.6%). Following closely was the endometrioid subtype, with a total of 6 cases (19.4%). The mucinous subtypes represented a total of four cases (12.9%). Conversely, the clear cell subtypes and undifferentiated subtypes were less prevalent, with a total of three cases (9.7%) and two cases (6.5%) respectively **(Figure 1)**.

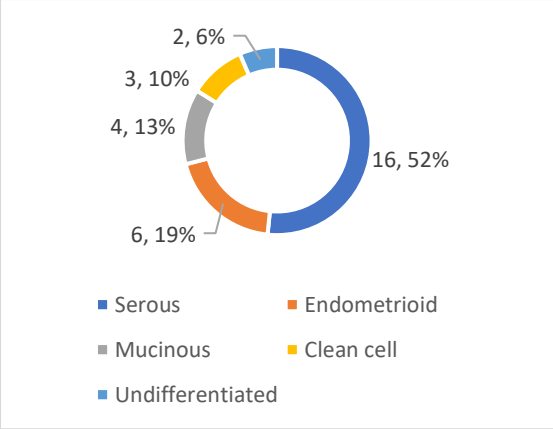

Figure 1: Distribution of histologic subtypes (N=31)

Turning to the distribution of WT1 scores across all 31 cases, it was observed that the highest number of cases, 14 in total (45.2%), displayed scores exceeding 50% (3+). Meanwhile, 13 cases (41.9%) demonstrated scores of less than 1% (0 or negative scores). A single case (3.2%) exhibited scores ranging from 1% to 10% (1+), while three cases (9.7%) showcased scores spanning from 11% to 50% (2+) **(Table II)**.

Table II: Distribution of WT1 scores (N=31)

WT1 Scores	n	%
<1% (0 or -Ve)	13	41.9
1% - 10% (1+)	1	3.2
11% - 50% (2+)	3	9.7
>50% (3+)	14	45.2

Analyzing the distribution of histologic subtypes among all participants, it became apparent that WT1 expression was predominantly observed in cases of serous carcinoma. Notably, all 16 instances of serous carcinoma (100%) exhibited a positive reaction for WT1. Within this subset, 14 cases (87.5%) presented WT1 scores surpassing 50% (3+), while the remaining two cases (12.5%) showcased scores spanning 11% to 50% (2+). In contrast, concerning endometrioid carcinoma, four out of six cases (66.6%) demonstrated a lack of WT1 expression, whereas one case (16.6%) exhibited a WT1 score of 1% to 10% (1+), and another case (16.6%) displayed a WT1 score ranging from 11% to 50% (2+). All four mucinous carcinoma cases (100%) and all three clear cell carcinoma cases (100%) yielded negative WT1 results, with staining of tumor cells accounting for less than 1%. Additionally, both cases (100%) of undifferentiated carcinoma exhibited negative WT1 expression. An interesting finding emerged, showing a significant relationship between WT1 expression and various histologic subtypes of epithelial ovarian carcinoma, confirmed by a calculated P value of 0.001 ($P < 0.05$) **(Table III)**.

Table III: WT1 expression in different histologic subtypes (N=31)

Histologic subtype	n	Positive cases	Negative cases

		1%-10%	**11%-50%**	**>50%**	**<1%**
Serous	16	0 (0%)	2 (12.5%)	14 (87.5%)	0 (0%)
Mucinous	4	0 (0%)	0 (0%)	0 (0%)	4 (100%)
Endometrioid	6	1 (16.6%)	1 (16.6%)	0 (0%)	4 (66.6%)
Clean cell	3	0 (0%)	0 (0%)	0 (0%)	3 (100%)
Undifferentiated	2	0 (0%)	0 (0%)	0 (0%)	2 (100%)

Within this study, an investigation into the relationship between WT1 scores and the subjects' ages was undertaken. Notably, the age group spanning 51 to 60 years exhibited the highest frequency of positive staining. Among the cases within this age group, six out of nine cases (66.6%) displayed WT1 scores exceeding 50% (3+). Moreover, one case (11.1%) out of nine presented scores ranging from 11% to 50% (2+), and another case (11.1%) demonstrated a WT1 score of 1% to 10% (1+). Solely one case (11.1%) exhibited negative staining in this age group. Conversely, among subjects aged between 20 to 30 years, a notably higher proportion showed negative staining. Specifically, five out of six cases (83.3%) were negative for WT1 expression, while only one case (16.6%) displayed WT1 scores spanning 11% to 50% (2+). Interestingly, despite these observations, the statistical analysis determined that there was no significant relationship between WT1 expression and the age groups, with a calculated P value of 0.220 ($P > 0.05$) **(Table IV)**.

Table IV: Relation of WT1 scores with age of the subject (N=31)

WT1 scores	**20-30**	**31-40**	**41-50**	**51-60**	**>61**	**Total**
<1% (0 Or -Ve)	5 (83.3%)	4 (50%)	2 (40%)	1 (11.1%)	0 (0%)	12 (38.7%)
1-10 % (1+)	0 (0%)	0(0%)	0 (0%)	1 (11.1%)	0 (0%)	1 (3.2%)
11-50% (2+)	1 (16.6%)	0 (0%)	0 (0%)	1(11.1%)	1(33.3%)	3 (9.6%)
>50% (3+)	0 0 (0%)	4 (50%)	3 (60%)	6 (66.6%)	2 (66.6%)	15 (48.3%)
Total	6	8	5	9	3	31
Percentages of total	19.40%	25.80%	16.10%	29.00%	9.70%	100%

Among the various subtypes, the serous subtypes exhibited the highest WT1 expression (>50% in 14 out of 16 cases). Conversely, the mucinous (4 out of 4), clear cell (3 out of 3), endometrioid (4 out of 6), and undifferentiated (2 out of 2) subtypes demonstrated the lowest WT1 expression (<1%) **(Figure 2)**.

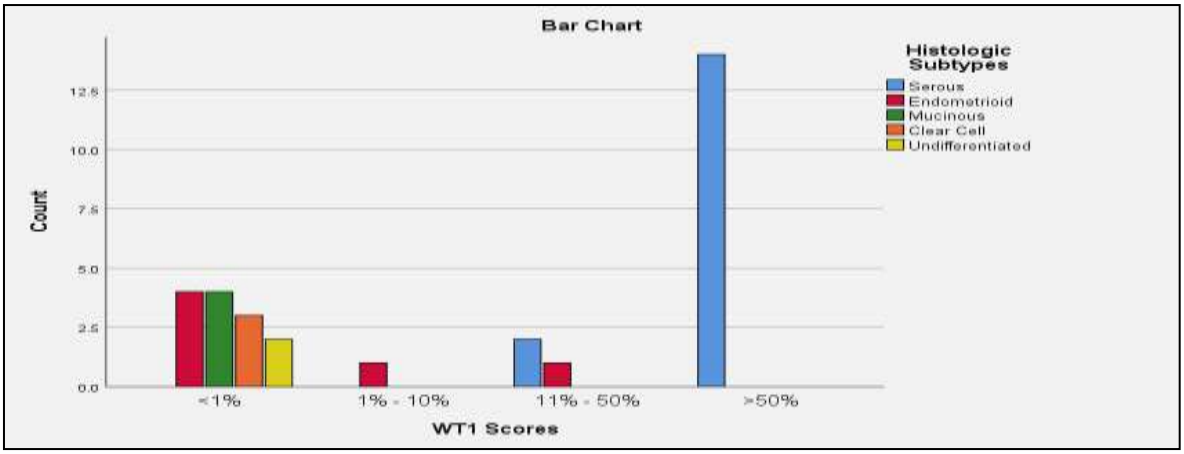

Figure 2: Frequency of expression of WT1 in different histologic subtypes

DISCUSSION

This study aimed to assess the relation of Wilms tumor 1 score with the age of ovarian carcinoma patients. The study sample encompassed individuals aged 20 to 75 years. Within the 31 instances of ovarian epithelial carcinoma examined, the median age was 47 years. The majority of cases (29%) fell within the 51-60-year age bracket. The subsequent most common age category was 31-40 years (25.8%). This outcome aligns with the findings from previous studies conducted by M Arab et al. and by Hwang et al. [14,15]. The current investigation observed no substantial correlation between patient age and the extent of WT1 expression (P-Value>0.05). This outcome mirrors the findings of Hafedh et al. in 2015 and Tanaka et al. in 2007, both of which demonstrated the absence of a significant association between age and WT1 expression [16,17]. In this study, among ovarian carcinomas, serous carcinomas exhibited the highest frequency of immune reactivity to WT1. All of the serous carcinomas included in our analysis displayed positive reactivity. This outcome is consistent with the findings reported by Goldstein et al. and Al-Hussaini et al. [18,19]. In this study, all instances of mucinous and clear cell carcinomas exhibited negative results for WT1 expression. This discovery aligns with the outcomes presented by Hashi et al. [20]. In contrast, Shimizu et al. in 2000 identified certain instances of immunohistochemical WT1 expression within both mucinous and clear cell carcinomas. The variations in WT1 expression observed among the serous, clear cell, and mucinous subtypes substantiate the findings of other investigations suggesting that immunohistochemical WT1 expression is indicative of biological cell type rather than mutations, as noted by Bruening et al. [21]. As proposed by Gilks in 2004, the diverse subtypes of epithelial ovarian carcinoma diverge in terms of gene expression profiles and biological behaviors [22]. This concept could elucidate the disparate WT1 expression patterns observed among these subtypes. All of the undifferentiated ovarian carcinomas examined in the present study exhibited no WT1 expression, contrasting with the findings of Waldstrom and Grove in 2005 where 80% of undifferentiated carcinomas had no WT1 expression, while the remaining 20% displayed diffuse positivity

[23]. This contrast in results might signify that certain histologically undifferentiated carcinoma are poorly differentiated serous (or endometrioid) carcinomas, whereas the WT1-negative carcinomas could belong to different biological cell types. The absence of WT1 expression may point towards ovarian tumors originating from endometriosis foci, as proposed by Barcena and Olive in 2011, suggesting distinct underlying pathogenic processes [24]. WT1 negativity helps distinguish serous ovarian carcinomas with morphological resemblance to pure clear cell ovarian carcinomas, as these latter cases are WT1 negative, according to McCluggage in 2008 [25]. Comparing the outcomes of this study with other recent investigations focused on WT1 in various subtypes of ovarian epithelial tumors, the analysis indicates consistent concordance with the majority of those studies.

LIMITATION OF THE STUDY

The study's sample size was limited in scope, potentially affecting the generalizability of its findings. Since the samples were solely obtained from RMCH, the outcomes might not accurately represent the broader population across the entire country. Furthermore, the study's brief duration could have implications for the comprehensive understanding of the subject under investigation.

CONCLUSION & RECOMMENDATION

The analysis conducted indicates that there is no statistically significant correlation between Wilms tumor 1 (WT1) scores and the age of patients diagnosed with ovarian carcinoma. In other words, as the age of ovarian carcinoma patients varies, the corresponding WT1 scores do not exhibit any consistent pattern of increase or decrease. This lack of a significant relationship suggests that the expression of WT1, as measured by its scores, does not appear to be influenced by the age of the patients afflicted with ovarian carcinoma. This finding implies that other factors or variables might be more influential in determining the variations observed in WT1 scores among these patients.

FUNDING

No funding sources

CONFLICT OF INTEREST

None declared

ETHICAL APPROVAL

The study was approved by the Institutional Ethics Committee

REFERENCES

1. *Rosai J. Rosai and Ackerman's surgical pathology e-book. Elsevier Health Sciences; 2011 Jun 20.*
2. *Standring S, editor. Gray's anatomy e-book: the anatomical basis of clinical practice. Elsevier Health Sciences; 2021 May 22.*
3. *He L, Wang Q, Zhao X. Microvessel density as a prognostic factor in ovarian cancer: a systematic review and meta-analysis. Asian Pacific Journal of Cancer Prevention. 2015;16(3):869-74.*
4. *Liu Z, Yamanouchi K, Ohtao T, Matsumura S, Seino M, Shridhar V, Takahashi T, Takahashi K, Kurachi H. High levels of Wilms' tumor 1 (WT1) expression were associated with aggressive clinical features in ovarian cancer. Anticancer research. 2014 May 1;34(5):2331-40.*
5. *Ferlay J, Soerjomataram I, Dikshit R, Eser S, Mathers C, Rebelo M, Parkin DM, Forman D, Bray F. Cancer incidence and mortality worldwide: sources, methods*

and major patterns in GLOBOCAN 2012. International journal of cancer. 2015 Mar 1;136(5):E359-86.

6. *Kurman RJ, Shih IM. The origin and pathogenesis of epithelial ovarian cancer-a proposed unifying theory. The American journal of surgical pathology. 2010 Mar;34(3):433.*
7. *Li J, Fadare O, Xiang L, Kong B, Zheng W. Ovarian serous carcinoma: recent concepts on its origin and carcinogenesis. Journal of hematology & oncology. 2012 Dec;5:1-1.*
8. *Vergara D, Merlot B, Lucot JP, Collinet P, Vinatier D, Fournier I, Salzet M. Epithelial–mesenchymal transition in ovarian cancer. Cancer letters. 2010 May 1;291(1):59-66.*
9. *Thomassin-Naggara I, Bazot M, Daraï E, Callard P, Thomassin J, Cuenod CA. Epithelial ovarian tumors: value of dynamic contrast-enhanced MR imaging and correlation with tumor angiogenesis. Radiology. 2008 Jul;248(1):148-59.*
10. *Kmet LM, Cook LS, Magliocco AM. A review of p53 expression and mutation in human benign, low malignant potential, and invasive epithelial ovarian tumors. Cancer. 2003 Jan 15;97(2):389-404.*
11. *Wheeler DT, Bell KA, Kurman RJ, Sherman ME. Minimal uterine serous carcinoma: diagnosis and clinicopathologic correlation. The American journal of surgical pathology. 2000 Jun 1;24(6):797-806.*
12. *Ceccaroni M, Chieco P, Alboni C, De Iaco P, Pagano K, Ceccarelli C, Santini D, Taroni B, Pelusi G. p53 expression, DNA ploidy and mitotic index as prognostic factors in patients with epithelial ovarian carcinoma. Tumori Journal. 2004 Nov;90(6):600-6.*
13. *Shimizu M, Toki T, Takagi Y, Konishi I, Fujii S. Immunohistochemical detection of the Wilms' tumor gene (WT1) in epithelial ovarian tumors. International journal of gynecological pathology. 2000 Apr 1;19(2):158-63.*
14. *Arab M, Khayamzadeh M, Tehranian A, Tabatabaeefar M, Hosseini M, Anbiaee R, Golfam F, Akbari ME. Incidence rate of ovarian cancer in Iran in comparison with developed countries. Indian journal of cancer. 2010 Jul 1;47(3):322-7.*
15. *Hwang JY, Lim WY, Tan CS, Lim SL, Chia J, Chow KY, Chay WY. Ovarian Cancer Incidence in the Multi-Ethnic Asian City-State of Singapore 1968-2012. Asian Pacific Journal of Cancer Prevention: APJCP. 2019;20(12):3563.*
16. *Hafedh MI, Ali SA, Talal LF. The role of Wilm's Tumor1 immunohistochemical marker in surface epithelial ovarian tumors. Journal of the Faculty of Medicine Baghdad. 2015 Jul 1;57(2):145-50.*
17. *TANAKA K, IKEDA M, SONOO H, HIRONO M, NOMURA T, OHKUBO S, YAMAMOTO Y, SHIIKI S, NAKAJIMA K, KUREBAYASHI J. The Relationship between Wilms' Tumor 1 (WT1) and Paired Box 8 (Pax-8) Protein Expressions in Papillary and Anaplastic Thyroid Carcinomas. 川崎医学会誌= Kawasaki medical journal. 2007;33(1):23-33.*
18. *Goldstein NS, Bassi D, Uzieblo A. WT1 is an integral component of an antibody panel to distinguish pancreaticobiliary and some ovarian epithelial neoplasms. American journal of clinical pathology. 2001 Aug 1;116(2):246-52.*
19. *Al-Hussaini M, Stockman A, Foster H, McCluggage WG. WT-1 assists in distinguishing ovarian from uterine serous carcinoma and in distinguishing between serous and endometrioid ovarian carcinoma. Histopathology. 2004 Feb;44(2):109-15.*
20. *Hashi A, Yuminamochi T, Murata SI, Iwamoto H, Honda T, Hoshi K. Wilms tumor gene immunoreactivity in primary serous carcinomas of the fallopian tube, ovary, endometrium, and peritoneum. International journal of gynecological pathology. 2003 Oct 1;22(4):374-7.*
21. *Bruening W, Gros P, Sato T, Stanimir J, Nakamura Y, Housman D, Pelletier J. Analysis of the 11p13 Wilms' Tumor Suppressor Gene (WTI) in Ovarian Tumors. Cancer investigation. 1993 Jan 1;11(4):393-9.*

22. *Gilks CB. Subclassification of ovarian surface epithelial tumors based on correlation of histologic and molecular pathologic data. International journal of gynecological pathology. 2004 Jul 1;23(3):200-5.*
23. *Waldstrøm M, Grove A. Immunohistochemical expression of Wilms tumor gene protein in different histologic subtypes of ovarian carcinomas. Archives of pathology & laboratory medicine. 2005 Jan 1;129(1):85-8.*
24. *Bárcena C, Oliva E. WT1 expression in the female genital tract. Advances in Anatomic Pathology. 2011 Nov 1;18(6):454-65.*
25. *McCluggage WG. Immunohistochemical markers as a diagnostic aid in ovarian pathology. Diagnostic histopathology. 2008 Aug 1;14(8):335-51.*