



GENETIC MARKERS IN GYNECOLOGIC ONCOLOGY: UNDERSTANDING HEREDITARY RISKS AND MUTATIONS

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Abstract

The research question of the study is the patterns of the risk of hereditary cancer and the awareness of genetic markers in women undergoing gynecologic evaluation. A questionnaire with a structured questionnaire was used to gather primary data by the administration of a questionnaire to ninety respondents to evaluate their knowledge of BRCA and mismatch repair mutation, previous genetic testing, and perceived cancer risk. The findings showed that the percentage of the participants who reported a family history of breast, ovarian, endometrial or colorectal cancer was quite high, which implied that the participants had a hereditary predisposition. The awareness of BRCA mutations exceeded that of mismatch repair defects, but clinically performed pathogenic mutations were detected in only a small proportion of the respondents. There was different risk perception where most of the participants perceived themselves to be moderate risk. These results indicate that awareness of hereditary cancer is growing but there are still gaps in the knowledge on the genetic pathways and genetic testing. The improvement of prevention and individualized therapy in gynecologic oncology is necessary through the strengthening of genetic counseling, the development of diagnostic services, and the promotion of early assessment of hereditary risks.

Keywords: hereditary cancer, gynecologic oncology, BRCA mutations, mismatch repair deficiency, genetic risk, primary data, molecular markers

1. Introduction

The gynecologic cancers, such as ovarian, endometrial, cervical, vulvar, and vaginal cancers, are a tremendous burden to the world, and hereditary predisposition is becoming immensely more prominent in their occurrence. The development of cancer genomics has shown that a significant number of gynecologic cancers occur as a result of inheriting mutations that predispose individuals to heightened lifetime risks. This inherited factor has become more pronounced in ovarian and endometrial cancer in which germline changes in genes that regulate DNA repair and genomic stability directly cause tumor formation and progression. Knowledge of such hereditary pathways is hence crucial towards early diagnoses, decrease in risk and tailored therapeutic interventions. Andrews and Mutch point out that hereditary ovarian cancer is a unique clinical condition, which demands specific prevention and monitoring strategies (Andrews and Mutch, 2017).

Genetic mutation, that is, BRCA1 gene, BRCA2 gene, and mismatch repair (MMR) gene defects, have become significant predictors of cancer risk as well as clinical outcome. Recent scientific studies have been targeted at predictive biomarkers, which can be used to influence diagnosis, choice of therapy and prognostication. Carvalho and Carvalho note that the lack of mismatch repair in endometrial cancer is a complex issue, which can be used as a predictive and diagnostic biomarker (Carvalho and Carvalho, 2024). On the same note, BRCA-related pathways are also associated with hereditary breast and gynecologic cancer syndromes and have an impact on the biology of tumors and therapeutic options. Chung and colleagues present an extensive review of BRCA-related hereditary syndromes, demonstrating the extensive consequences of the germline modifications in the case of various types of gynecologic cancer (Chung et al., 2020).

Gynecologic cancers have developed drastically in terms of their molecular terrain due to the integration of genomic classification systems. In the case of endometrial cancer, the replacement of conventional histopathology by molecularly informed categories has gone a long way in enhancing a more accurate diagnosis and a more effective therapeutic orientation. Concin and colleagues offer new international standards that define the role of molecular classification in the treatment of endometrial carcinoma, a significant step towards precision medicine (Concin et al., 2021). This has also improved risk stratification due to the identification of unique molecular subtypes. Daly et al. also highlight the importance of family history and inherited gene mutations to narrow down one-on-one cancer surveillance and prevention programs and show the use of this mode in the ovarian and endometrial cancer pathways (Daly et al., 2020).

The latest developments in staging systems continue to incorporate genetic information in the clinical decision-making. Recent staging guidelines on endometrial cancer have incorporated the molecular aspects including POLE mutations and p53 abnormalities, and this represents the expanding use of genomics in practice. Gaffney and colleagues explain that today staging models are more and more based on the use of genetic modifications to enhance prediction of the outcome (Gaffney et al., 2024). Hereditary breast and ovarian cancer (HBOC) syndromes are constantly under development and research is no longer limited to BRCA1/2 mutations. Hoang and Gilks point out more genes that play a role in hereditary cancer vulnerability, and the hereditary gynecologic oncology spectrum is growing (Hoang & Gilks, 2018).

The introduction of molecular pathology has reshaped the concept of tumor behavior, as it has become possible to understand the carcinogenic pathways better. Jamieson and colleagues point out the increasing role of the molecular pathology in informing personalized treatments of cancers of the gynecology (Jamieson et al., 2021). Likewise, tumor signature studies have offered fresh clues of the association of genetic cancer genes and the development of certain gynecologic tumors. According to Kondrashova et al., tumor genomic signatures are able to reveal hereditary predispositions underlining endometrial cancer (Kondrashova et al., 2021). These results reinforce the requirement of genetic analysis on patients who show a specific tumor pattern of molecular origin.

Recent recommendations emphasize the value of hereditary cancer syndrome detection methods based on early and accurate germline and somatic tumor testing. Konstantinopoulos and colleagues emphasize that genetic testing must be used in ovarian cancer, and in this case, the identification of germline mutations has both therapeutic and prognostic direct consequences (Konstantinopoulos et al., 2020). Kostov et al. introduce an expanded perspective on hereditary gynecologic cancer syndromes, which include a list of genetic and clinical characteristics of the inherited disorders (Kostov et al., 2022). Molecular classification has also been proved to be a strong prognostic factor in high-risk endometrial cancer. Leon-Castillo and the TransPORTEC Consortium disclose that the combination of molecular markers enhances the prediction of the response to treatment and the general prognosis (Leon-Castillo et al., 2020).

Combining all of this evidence, it is clear that hereditary mutations and molecular markers are the focal point of contemporary gynecologic oncology. They support risk of disease, direct the diagnostic assessment, affect the treatment choice, and define preventive measures. Although much has been achieved, there are still gaps in the knowledge of how the mechanisms of hereditary cancer interact in various malignant diseases of the gynecology setting. The proposed study will attempt to review

the existing evidence and add to the broader knowledge about hereditary genetic markers in gynecologic oncology.

2. Methodology

2.1 Study Design

The research design applied in this study was descriptive, cross-sectional research design with only primary data collection. This design enabled direct evaluation of the indicators of hereditary cancer risk, awareness of genetic mutation, and allocation of hereditary traits in women under gynecologic assessment. The use of all primary data to the full extent made sure that the results were the present risk patterns in the target population and were not based on the external data. The research was done at Barasat Government Medical College, Barasat, North 24 Parganas, Kolkata, which is one of the leading tertiary care centers delivering gynecologic and oncology services to a heterogeneous group of patients.

The study period was one year and the study was carried out between December 2024 and January 2024. The one year was sufficient to ensure that the participants were recruited in the gynecologic screening and oncology outpatient departments and that variations in patient flow across months could be taken into consideration and that the group of participants represented the general trends of clinical life of the whole year.

2.2 Study Population and Sample Size

The sample population comprised of 90 women who were recruited in gynecologic screening units, oncology outpatient services and hereditary cancer counseling clinics. The sample was chosen so as to have sufficient individuals with possible hereditary cancer risk factors including those who had personal or family histories that were indicative of genetic susceptibility. Women who gave informed consent and were aged eighteen years or above were only included. Those who refused to take part or gave limited information were locked out to ensure quality of data. A total of 90 women were finally recruited with the sample size being decided by the feasibility sampling which was arrived at by considering the number of patients who were expected to pass through the hospital and the population of eligible participants during the study duration. This strategy provided sufficient representation of the target population and enabled any descriptive analysis that was meaningful within the limitations of a cross-sectional study design.

2.3 Data Collection Procedure

A structured questionnaire that was self-administered by the researcher was used to gather primary data. The questionnaires were filled in a monitored environment in order to bring out perfect sense and precise answers. The questionnaire used was able to include demographic data, personal gynecologic history, family cancer history, knowledge of hereditary cancer syndromes, and genetic testing experiences, and the presence of clinically diagnosed mutations where appropriate. Verification of reported clinical or genetic information was done by the medical documentation of participants where possible, to increase the accuracy.

2.4 Data Variables and Classification

The main data set included demographic features, clinical history, family history of genetic cancer, and self-reports or clinically proven genetic features. Independent variables were personal diagnosis of gynecologic cancer, family history of breast, ovarian, endometrial, and colorectal cancers, knowledge of BRCA and mismatch repair genes mutations, prior genetic testing, and hereditary cancer belief. Behavioral factors like readiness to be screened genetically and the perception towards preventive measures were also factored in. Each study variable was coded in a systematic manner.

2.5 Data Analysis

The analysis of the data and statistical analysis of the study were done in Microsoft Excel. Data was entered and variables coded using Microsoft Excel, data were cleaned by the questionnaire responses and they were then organized into a format that could be analyzed. The software also facilitated the calculation of the descriptive statistics, frequency distribution, and percentage analysis which were imperative in the interpretation of the level of awareness, family history pattern and indicators of hereditary cancer risks of the participants. The accuracy, transparency and reproducibility of the statistical procedures as well as the streamlined workflow of the study (descriptive cross-sectional research design) were met by the use of Microsoft Excel.

2.6 Ethical Considerations

The research was conducted in a morally acceptable way. All the participants were notified about the purpose of the study and given free consent before inclusion. The anonymity and confidentiality were carefully observed and no identifiable details were noted in the dataset. The paper followed established ethical standards of research on human subjects since the nature of the proposed research was limited to the use of questionnaires with the lowest risk of causing harm.

3. Results

3.1 Overview of the Study Participants

There were a total of ninety women who participated in the study. The sample gives a varied representation of the age, reproduction, family history of cancer, and awareness about hereditary cancer predictors. The findings of the descriptive analysis give an understanding of the commonality of hereditary cancer risk patterns in women who receive gynecologic and oncology services. In order to describe the demographic traits of the participants, Table 1 generalizes age distribution and the essential clinical data of the respondents.

Table 1. Demographic Characteristics of the Participants (n = 90)

Variable	Category	Frequency (n)	Percentage (%)
Age Group	18–30 years	22	24.4%
	31–45 years	36	40.0%
	46–60 years	24	26.7%
	Above 60	8	8.9%
Menopausal Status	Premenopausal	48	53.3%
	Postmenopausal	42	46.7%
Parity	Nulliparous	18	20.0%
	Multiparous	72	80.0%

The demographical data show that most of the participants were aged 31 to 45, and over 50% of them were premenopausal. The fact that the majority of them were multiparous also implies that the reproductive population is relatively experienced, something characteristic of a gynecologic screening cohort.

3.2 Family History of Cancer

The family history is one of the primary elements of hereditary cancer risk evaluation. The participants were questioned in this research to provide information about the known history of cancer in the first or second degree of relatives. The reported family cancer history is also given in Table 2.

Table 2. Distribution of Family Cancer History Among Participants

Cancer Type in Family	Frequency (n)	Percentage (%)
Breast Cancer	28	31.1%
Ovarian Cancer	12	13.3%
Endometrial Cancer	8	8.9%

Colorectal Cancer	14	15.6%
No Family History Reported	28	31.1%

The statistics show that almost one-third of the participants have reported family history of breast cancer, and ovarian, endometrial, and colorectal cancer were also reported among family. A third of the respondents indicated that there was no history of any cancer in their family. The occurrence of hereditary cancer syndromes like HBOC and Lynch syndrome shows their importance in this group of people.

3.3 Awareness of Genetic Mutations

The patients were questioned on the knowledge of specific mutations of hereditary cancers such as BRCA1/2 and mismatch repair genes linked to Lynch syndrome. Figure 1 shows the general knowledge of genetic mutations in the participants before giving the detailed results.

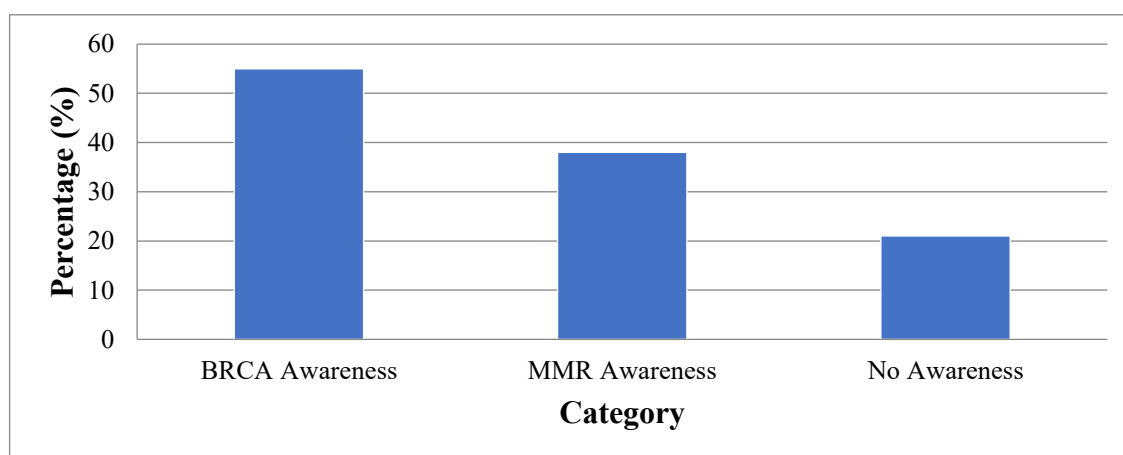


Figure 1. Awareness of Major Hereditary Cancer Mutations (BRCA, MMR)

The figure indicates that 55% of the participants were familiar with BRCA mutation and 38 percent familiar with mismatch repair gene mutation. A significant proportion (21) indicated that they were unaware of hereditary mutations, which proves that more intensive genetic education programs are needed. To augment this figure, Table 3 shows mutation awareness in more finer classification.

Table 3. Awareness and Understanding of Hereditary Genetic Mutations

Awareness Category	Frequency (n)	Percentage (%)
Aware of BRCA1/BRCA2 only	30	33.3%
Aware of MMR genes only	8	8.9%
Aware of both mutation types	22	24.4%
Not aware of any mutations	30	33.3%

According to the table, a third of the women knew about BRCA mutations only, whereas a smaller group of women knew about MMR defects only. A quarter of them showed familiarity with both hereditary pathways whereas a third was not aware at all.

3.4 Prevalence of Clinically Documented Mutations

The participants who had undergone genetic testing previously or reported hereditary profile were requested to indicate the occurrence and absence of confirmed mutation. The findings are presented in Figure 2 below.

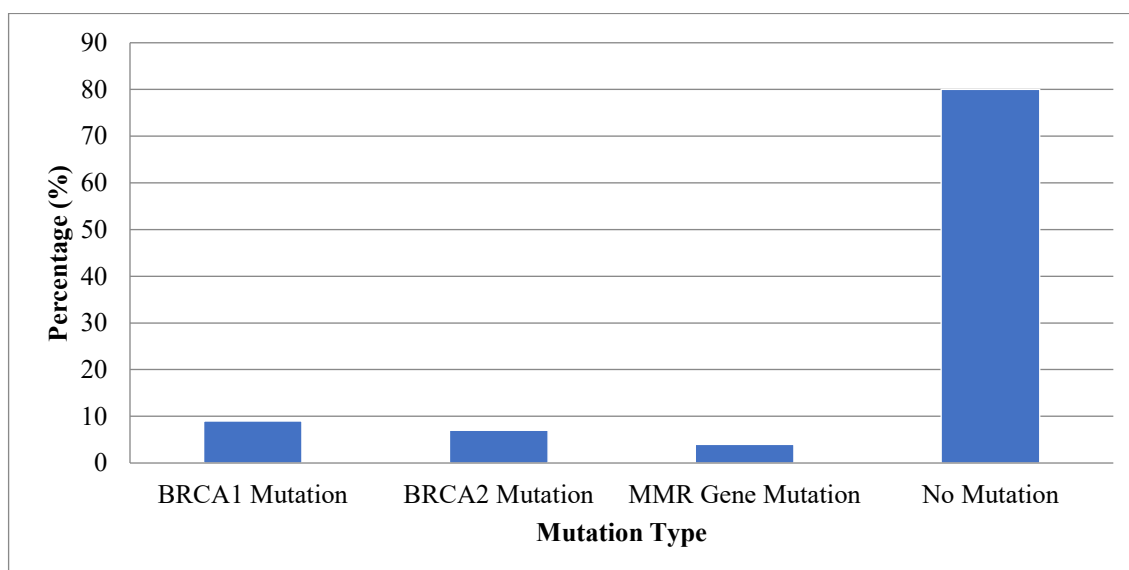


Figure 2. Distribution of Clinically Documented Hereditary Mutations

The result indicates that hereditary mutations were reported in a small percentage of subjects. BRCA1 and BRCA2 mutation was detected in 9 and 7 percent of participants respectively and 4 percent of the participants had mismatch repair defects. Most (80%) of them did not have any confirmed mutations according to population level expectations.

3.5 Perception of Personal Cancer Risk

Psychological and behavioral tendencies were measured through the perception of the participants of hereditary risk. Table 4 indicates the perceived risk of cancer among the 90 respondents.

Table 4. Perception of Personal Cancer Risk Among Participants

Perceived Risk Level	Frequency (n)	Percentage (%)
Low Risk	26	28.9%
Moderate Risk	42	46.7%
High Risk	22	24.4%

The findings suggest that almost half of the participants said they considered themselves moderate risk of having hereditary cancer and almost a quarter of them scored their risk as being high. The trend is in accordance with the family cancer history and the mutation awareness trends. In order to visually complement these findings, Figure 3 demonstrates the percentage of the perceived level of risks among the participants.

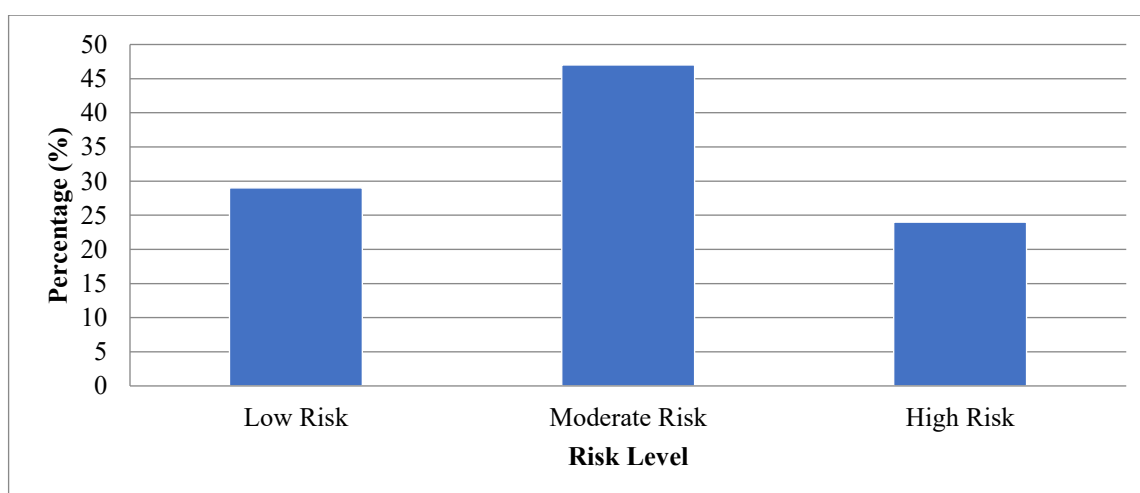


Figure 3. Participants' Perceived Hereditary Cancer Risk

Figure 3 illustrates that moderate-risk perception was the most widespread meaning that general awareness of possible hereditary predisposition was even in people who were not known to have genetic mutations. In general, the findings demonstrate that the risk factors of hereditary cancer have a significant representation in the research sample. A large share of the participants had a relevant family history in terms of breast, ovarian, endometrial, or colorectal cancers and over fifty percent of the participants showed knowledge of BRCA mutations. Though only a minority were clinically diagnosed with genetic mutation cases, many of them felt that they had moderate to high risks of having hereditary cancer. All these trends point towards the necessity of enhancing the education of hereditary cancer, greater access to genetic testing, and enhancing the detection of risk at an early stage in women visiting gynecologic care.

4. Discussion

The findings of the study reveal that the risk factors of hereditary cancer do exist amongst a significant number of women seeking gynecologic assessment. The results, especially the significant family history of breast, ovarian, endometrial, and colorectal cancer among the participants can be discussed as being consistent with the existing evidence regarding the hereditary element of gynecologic cancer. According to Lheureux and colleagues, epithelial ovarian cancer often has an underlying background of germline mutations and that clinical treatment still develops as a result of the development of precision medicine (Lheureux et al., 2019). This helps to confirm the trends in the current research, as the understanding of hereditary risk was the highest among those who cared about ovarian cancer. The gynecologic cancers classification of their molecular classification has gradually begun to affect the diagnostic and therapeutic decisions. The results of the current study concerning the principles of awareness of mismatch repair mutations and POLE aberrations among the respondents are indicative of the changes in molecular taxonomy. According to Loukovaara and colleagues, molecular classification has made endometrial cancer a genomically stratified disease entity, which is now treated more personally (Loukovaara et al., 2022). This change in attitude towards the importance of underlying molecular abnormalities in prognosis is in line with the moderate-to-high risk perception in the participants.

BRCA1 and BRCA2 are genetic factors as well as mismatch repair genes which have found significant roles in the assessment of hereditary gynecologic cancers. The comparatively small size of the population with clinically confirmed mutations in the current study is not surprising to the population-based cohort design; nevertheless, the rates of awareness of BRCA and MMR genes show the growing experience of the population with the education about the hereditary cancer. Lu and Broaddus depict in detail the mechanisms of abnormalities in the molecules that dictate the behavior of endometrial cancer and influence clinical interventions (Lu and Broaddus, 2020). This strengthens the relationship between mutation awareness and clinical knowledge among the subjects.

Another important point raised by a considerable number of respondents was their worry about their personal risk of cancer, which suggests that predictive biomarkers have a potentially important role in patient behavior and decision-making. According to Nagel and others, predictive biomarkers will become an inseparable component of the work of a pathologist, allowing more accurately identify hereditary risk and improve the accuracy of the diagnosis of gynecologic cancer (Nagel et al., 2024). The statistics of the study imply that a significant amount of women are aware of the consequences of hereditary mutations, even though they have never had a genetic test done on themselves.

The advantageous aspect of another dimension of hereditary gynecologic cancer is that it is instability of the tumor based on genomics, especially in cervical carcinogenesis. Porter and Marra prove that the instability of the genome, particularly in the case of HPV-related cancers, has substantial effects on the development of tumors and their clinical outcome (Porter and Marra, 2022). Despite the fact that the issue of cervical cancer was not the highest among the respondents, the results of the mutation awareness and the family history indicate the importance of further genomic screening of all gynecologic cancers.

The fact that many of the participants have a family history indicates that familial cancer syndromes are not adequately perceived and identified in clinical practice. Purohit and others outline the importance of researching the contribution of a broad collection of genetic variants to hereditary gynecologic cancers in addition to the importance of systematic assessment of individuals at risk (Purohit et al., 2024). This is in line with the observation of the study that a sizeable percentage of the respondents considered themselves at the moderate or high risk because of their family backgrounds. Their anxieties are justified since syndromes like hereditary breast-ovarian cancer and Lynch syndrome contribute to a significant portion of predisposition to gynecologic cancer.

The small percentage of respondents with validated pathogenic mutations indicates the real world issues around the accessibility and completion of genetic testing. However, there is a strong therapeutic value in the identification of such mutations. The study by Ray-Coquard et al. (2019) confirms the importance of homologous recombination-deficient ovarian cancer diagnosis by showing that the combination of olaparib and bevacizumab in women advances the overall outcomes of the treatment and, consequently, the patient population should be correctly diagnosed with the hereditary mutation. The findings of the current research also confirm the importance of incorporating hereditary risk evaluation into the regular gynecologic oncologic practice.

Overall mutation genome also illustrates the interaction of inherited and somatic mutation. According to Watanabe et al. somatic and inherited susceptibility genes are important determinants of multiple gynecologic malignancies and offer a genomic paradigm, which is relevant to the trends among participants (Watanabe et al., 2023). On the same note, Yao and colleagues also highlight the importance of homologous recombination repair gene mutations in the biology of ovarian cancer and their relationship with clinical phenotypes (Yao et al., 2022). These results demonstrate the relevance of a detailed genomic assessment that entails germline and somatic profiling.

Structured genetic counseling is necessary since the awareness levels and perceived risks in the study indicated this. Counseling helps women to learn the hereditary risk, correctly interpret the genetic test results, and make effective decisions concerning preventative measures. In hereditary gynecologic cancer syndromes, Zhao et al. focus on the role of risk assessment and fertility counseling in their study, which, according to the authors, requires the development of integrated care models that will consider both the genetic and reproductive issues (Zhao et al., 2025). This need is supported by the current study because numerous participants were not sure about their own susceptibility despite having an appropriate family history.

The research possesses a number of limitations that must be taken into consideration when explaining the results. Being a descriptive, cross-sectional study, it only records what was happening at one moment in time and thus one is unable to come up with a cause and effect relationship of hereditary cancer awareness and true genetic risk factors. The size of 90 participants is sufficient to perform a descriptive analysis but it might not be representative of the general population of women receiving gynecologic assessment, which will restrict the applicability of the findings. The study also depended on the data presented by the self-reported questionnaire which might add recall bias or personal and family cancer history question misrepresentation by the participants. The other notable limitation is the limited availability to clinically validated genetic testing reports which might have resulted in underestimation of actual prevalence of pathogenic hereditary mutations among the respondents. Irrespective of these constraints, the research will be useful in understanding hereditary cancer awareness and perception of risk in the target.

5. Conclusion

The paper emphasizes the important role of genetic factors in determining the risk of cancer in women who are subjected to gynecologic examination. Existence of family histories of breast, ovarian, endometrial, and colorectal cancers in the sample highlights the persistence of the use of hereditary cancer syndromes, including the HBOC and Lynch syndrome. Despite the comparatively high level of awareness on BRCA mutations, the level of awareness on mismatch repair gene defect and general hereditary pathways was relatively low. The percentage of individuals who had gone through genetic

testing or had clinically validated pathogenic mutations was very minimal, and this indicates that there is still a barrier to accessing genomic assessment. The differences in the individual cancer risk perception, which were seen in this study, also underline the significance of the systematic patient education and thorough genetic counseling. Since molecular classification and precision oncology is onwards, early detection of hereditary predisposition will exist as vital to enhancing prevention, surveillance and tailored therapy interventions. Enhancing clinical pathways to assess genetic risks, improving patient knowledge of genetic risks and increasing access to testing services would all help to enhance the outcomes of women at risk. In sum, the results can be used to justify the significance of hereditary cancer assessment within a standard gynecologic care model to aid in the detection and the subsequent treatment of genetically associated malignancies.

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