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Original Article

Are Quality Control Practices in Molecular Genetics Laboratories Good Enough for Ovarian Cancer Diagnosis in Resource-Limited Settings? A Study from Kazakhstan

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ABSTRACT

Introduction: Ovarian cancer is a major cause of cancer death in women, mostly due to late detection. Quality control (QC) in molecular genetics laboratories is essential for accurate testing of BRCA1/2 and other mutations. This study evaluated QC practices in molecular genetics laboratories in Kazakhstan conducting ovarian cancer diagnostics in a resource-limited setting and compared them with international standards. Aim: To assess the quality control practices of molecular genetics laboratories involved in ovarian cancer diagnostics in Kazakhstan.

Methods: A descriptive cross-sectional study was conducted among 25 laboratory employees from three molecular genetics laboratories in Almaty, Kazakhstan. The questionnaire assessed internal quality control (IQC), external quality assessment (EQA) participation, SOP compliance, and operational challenges. Data were analysed using SPSS v.28. A systematic literature review based on PRISMA 2020 guidelines was also performed.

Results: Daily use of positive and negative controls was reported by 68% of respondents, while 52% performed daily DNA quality checks and 60% reported full SOP compliance. Equipment calibration was conducted weekly or monthly (44% each) rather than daily. Major challenges included sample contamination (56%), unreliable reagents (48%), and inadequate funding (68%). EQA participation was 76%. Respondents recommended improved training (52%), automation (36%), and better sample handling (32%). The review indicated that daily controls, high-depth NGS, and automation achieved 98–99% accuracy in BRCA1/2 testing.

Discussion: QC practices in Kazakh laboratories are reasonable but reveal gaps in calibration frequency, sample integrity, and resources. Daily calibration, affordable automation, local EQA programs, and staff training could improve diagnostic accuracy in resource-limited settings.

Keywords: Ovarian Cancer; Molecular Diagnostics; Quality Control; BRCA1/2; Resource-Limited Settings

Introduction

Ovarian cancer has been among the top causes of death due to cancer in the female gender across the globe. In 2020, some 313,959 new cases were identified worldwide with 207,252 reported deaths [1]. The late-stage diagnosis is one of the primary reasons of poor prognosis since the initial symptoms of the disease, such as pelvic pain, bloating, and urinary frequency, are non-specific and often overlap with benign conditions [2,3]. High-grade serous carcinoma (HGSC) is the most aggressive subtype that presents specific diagnostic issues because of its asymptomatic course and the low sensitivity of common screening tests, including transvaginal ultrasound (TVUS) and cancer antigen 125 (CA-125) [4].

The field of molecular diagnostics has revolutionized the process of diagnosis and treatment of ovarian cancer. Next-generation sequencing (NGS) and polymerase chain reaction (PCR) can now be used to identify clinically-actionable mutations in genes such as BRCA1/2, TP53, and PIK3CA to guide targeted therapies including PARP inhibitors [5,6,7]. Non-invasive methods like circulating tumor DNA (ctDNA) and cell-free DNA (cfDNA) analysis also broaden the capabilities of early detection, but issues of cost and standardization remain [8,9].

Strong quality control (QC) systems are crucial to the reliability of molecular diagnostic results. The major aspects encompass internal quality control (IQC), external quality assessment (EQA), and adherence to the standard operating procedures (SOPs), and alignment with the international standards, such as ISO 15189 and the Minimum Information for Publication of Quantitative Real-Time PCR Experiments (MIQE) guidelines [10-15]. Although these frameworks have been extensively adopted in high-income countries, their implementation in low- and middle-income countries (LMICs) remains uneven. Although there has been an increasing interest in precision oncology in LMICs, empirical information on actual QC practices in molecular genetics laboratories conducting diagnostics for ovarian cancer in Central Asia and other resource-limited contexts is remarkably lacking. Existing literature, most of which is narrative reviews or studies in high resource settings, is very limited in terms of validation of frameworks in local settings [16 - 20]. As an upper-middle income country with developing molecular diagnostics capacity, Kazakhstan provides a good example to learn about challenges and opportunities in implementation of molecular diagnostics in LMICs. But there has been no systematic preexisting evaluation of QC procedures in Kazakh molecular laboratories involved in the testing of hereditary cancer.

The current study aims to fill this gap by assessing QC activities in molecular genetics laboratories for the diagnosis of ovarian cancer in Almaty, Kazakhstan. In order to achieve this, we employed a mixed-methods study design (cross-sectional survey of laboratory staff and systematic literature review) and set out to: evaluate current levels of IQC, EQA participation and SOP compliance; and identify key operational challenges; and make evidence-based recommendations relevant to resource-limited settings. The results provide practical recommendations to improve the reliability of diagnosis in LMICs and national initiatives on precision oncology.

Materials and Methods

Study Design and Setting

The study used a descriptive cross-sectional study design that was conducted between December 2024, and May 2025 in three molecular genetics laboratories in Almaty, Kazakhstan. Such laboratories are major regional centers of ovarian cancer molecular diagnostics, which entails the techniques of polymerase chain reaction (PCR) and next-generation sequencing (NGS), including the detection of mutations in BRCA1 and BRCA2 gene. The research was divided into two parts: a questionnaire survey of laboratory employees and a systematic literature review that was conducted in accordance with the Preferred Reporting Items to Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines [21].

Participants and Eligibility Criteria

The survey encompassed 25 lab staff including lab technicians, molecular biologist, and quality control (QC) managers who were directly or indirectly involved in ovarian cancer molecular diagnostics. Purposive sampling was adopted to select the participants because there are only a few specialized laboratories in the study area. To be eligible, an individual had to be actively engaged in some molecular diagnostic processes, such as PCR or NGS, and work within one of the chosen labs. People who were not involved in any diagnostic or QC-related activity or those who opted not to participate were excluded. All the participants, who were eligible, agreed to participate, and the response rate was 100%. No demographic information had been gathered (age,

sex, etc.), because the research was conducted in the field of professional experience and QC practices.

Laboratory Characteristics

Participating laboratories differed in sector, accreditation status, testing volume, and technological capacity as seen table 1 below.

Table 1. Characteristics of Participating Molecular Genetics Laboratories in Almaty, Kazakhstan

Characteristics	Laboratory 1	Laboratory 2	Laboratory 3
Sector	Public	Public	Private
Accreditation status	None	Partial ISO 15189	None
Approximate annual ovarian cancer samples tested	150–200	200–250	100–150
Primary testing techniques	PCR, NGS	PCR, NGS	PCR
Sequencing platform	Illumina MiSeq	Ion Torrent	N/A
BRCA1/2 testing volume per year	~140	~180–200	~80
Number of staff in molecular diagnostics	12	15	8
Average daily testing workload	Moderate	High	Low

Note: A total of 25 laboratory staff from these three laboratories participated in the survey.

Study Outcomes

The main study outcome was the quality control practices in the field of ovarian cancer molecular diagnostics, which is specifically the internal quality control (IQC), taking part in external quality assessment (EQA) programs, and adherence to standard operating procedures (SOPs). Secondary outcomes were the identification of critical issues impacting the implementation of QCs including sample integrity, equipment calibration, and reagent stability as well as the determination of the perceived effectiveness of QC measures and the development of recommendations to enhance the diagnostic reliability, especially in BRCA1/2 mutation testing.

Data Collection and Survey Instrument

Data were collected using a structured, self-administered questionnaire developed based on international laboratory quality standards (ISO 15189:2022, CLIA guidelines, EMQN best practices, and MIQE guidelines). The questionnaire consisted of 20 main items organized into five domains covering respondent information, current QC practices, challenges, training/standardization, and recommendations. Five laboratory professionals were used for pilot testing of the instrument. The entire questionnaire is available in Supplementary File 1.

Systematic Literature Review

A systematic literature review was undertaken to determine the similarities and differences between local QC practices and international standards in the area of molecular diagnostics in the diagnosis of ovarian cancer. The studies published between January 1, 2015 and April 30, 2025 were searched in electronic databases such as PubMed, Scopus, Web of Science and Google Scholar. The search strategy consisted of a combination of Medical Subject Headings (MeSH) and free-text terms using Boolean operators related to quality control, molecular diagnostics and ovarian cancer. Adaptations specific to the database were made and in the case of Google Scholar, the first 100 results ranked in terms of relevancy were filtered. A backward and forward citation tracking was also conducted in order to find more relevant studies [22]. The articles were selected based on the following criteria: the articles had to focus on quality control practices in molecular diagnostic techniques (such as PCR or NGS) and had to provide a clear and reproducible methodology. The exclusion criteria were: not related to ovarian cancer, not containing information about QC, not having a clear methodology, published prior to 2015, and not in English. 1200 records were first identified and by eliminating duplicates with EndNote X9, 900 records were left as distinct records. Two reviewers independently screened titles and abstracts to yield 250 articles being reviewed in detail. Out of them, 80 studies were eligible to participate in the study, and 30 high-quality studies with 80% or more points on the Critical Appraisal Skills Programme (CASP) checklist were included in the final synthesis. Eight studies were summarized in tabular form and the rest of the studies were summarized narratively. The data extracted consisted of the characteristics of the study, QC methods, diagnostic methods, accuracy and error rates, and key recommendations. Figure 1 below demonstrates how the systematic review process was conducted to find the studies regarding quality control mechanisms in molecular genetics laboratories used to perform the diagnostic procedures related to ovarian cancer [21].

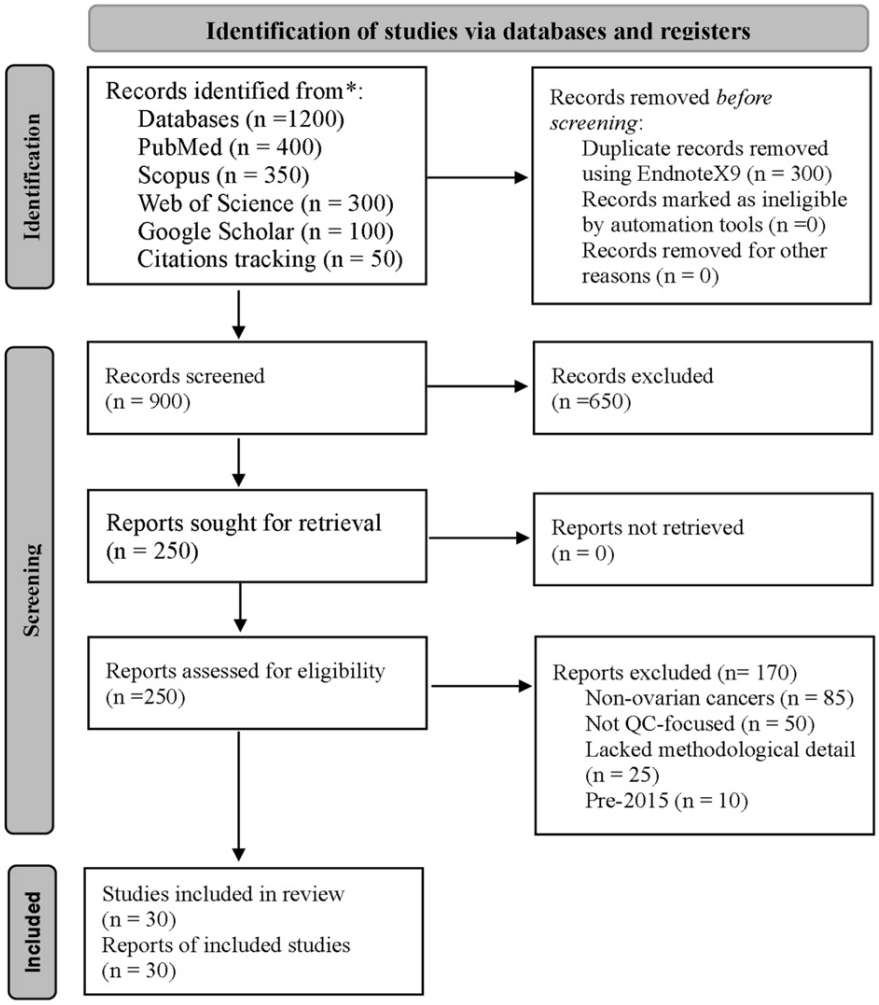

Figure 1 – PRISMA 2020 Flow Diagram

Figure 1. PRISMA 2020 Flow Diagram

Figure 1. PRISMA 2020 flow diagram showing identification, screening, and inclusion procedure of studies in a systematic review on ovarian cancer and quality control. This figure has three crucial steps: Identification of studies through databases and registers (top), Screening of records (middle), and Included studies (bottom). It starts with the identification of records in databases (PubMed, Scopus, Web of Science, Google Scholar) and citations, continues with the screening of the relevance of the studies, and ends with the inclusion of the studies that meet the inclusion criteria. There are also certain numbers used in the review which amount to 1200 records being identified, 900 being screened following removal of duplicates, 250 assessed as eligible to reports and 30 studies following the inclusion criteria after application of duplication measures. The diagram depicts a simplified schematic structure. Based on Page et al 2021.

Statistical Analysis

The data of the surveys were analyzed by using the descriptive statistics and the results were presented in the form of frequencies and percentages to summarize existing QC practices and challenges. The statistical analysis was done using IBM SPSS version 28. No inferential statistical tests, no power calculations were done since the research was descriptive in nature and the sample size was fixed. The results of the systematic literature review were synthesized in a narrative way to reveal some common trends, challenges, and best practices in the implementation of QC.

Ethical Considerations

The study was ethically approved by the Local Ethics Committee of the Faculty of Medicine and Healthcare, Farabi University (approval number IRB-A996/5; IRB00010790; approval date December 26, 2024). Informed consent was obtained beforehand by all the participants and they were guaranteed anonymity and confidentiality. Participation was voluntary and the participants were free to quit at any point of the research. No biological samples or any recognizable personal information was gathered.

Results

Characteristics of Participating Laboratories and Respondents

The study involved staff from three molecular genetics laboratories in Almaty, Kazakhstan, with varying capacity and infrastructure. Twenty-five laboratory employees were involved, 8 of whom were laboratory technicians (32%), 7 molecular biologists (28%), 5 quality control managers (20%), and 5 others (20%). Regarding experience, 8 (32%) had >10 years, 6 (24%) had 6 –10 years, 6 (24%) had 1–5 years, and 5 (20%) had <1 year of relevant experience.

Notable Discoveries from studies on Quality Control Measures in Ovarian Cancer genetic testing

The systematic review identified consistent advances in QC for ovarian cancer genetic testing. NGS achieved 99% accuracy for BRCA1/2 testing in formalin-fixed paraffin-embedded (FFPE) samples at sequencing depths ≥40× [23,24,25]. Multigene panels demonstrated 95% concordance with Sanger sequencing, underscoring the need for standardisation [26,27]. Whole-genome sequencing (WGS) attained 98% sensitivity with standardised QC metrics [28,29]. EQA implementation with detection thresholds >10% enhanced BRCA1/2 accuracy [30], while 75% of US laboratories reported EQA participation [28]. The presented findings highlight the importance of the urgent introduction of the standard QC processes in the resource-constrained environment such as Kazakhstan. Major evidence summary is seen in Table 2 below.

Table 2. Summary of notable research on quality control (QC) measures in ovarian cancer genetic testing

Author(s)	Journal	Notable Discoveries
Strom et al., 2015	*PLOS ONE*	The Next Generation Sequence (NGS) assay for BRCA1/2 testing achieved 99% validation accuracy due to proper calibration procedures which enhanced laboratory reliability to detect rare alleles in assessments.
Lincoln et al., 2015	*The Journal of Molecular Diagnostics*	Multigene panels enhance detection through reliable quality control tests which reach a 95% match level to Sanger techniques and underline the importance of standardization for testing hereditary ovarian cancer.
O'Daniel et al., 2017	*Genetics in Medicine*	Lab analysis reporting in the United States shows 75% of facilities use EQA but uniform practices for ovarian cancer genetic testing should be established to improve consistency.
Marshall et al., 2020	*NPJ Genomic Medicine*	WGS validation requires performance metrics to reach 98% sensitivity through standard quality control examinations when performing thorough genetic analysis of ovarian cancer.
Grafodatskaya et al., 2021	*Journal of Medical Genetics*	Accuracy improvements through standardized testing of BRCA1/2 by applying EQA procedures at the 10% Low Level of Detection according to established guidelines and reporting standards.
Kim et al., 2023	*Taiwanese Journal of Obstetrics and Gynecology*	The precision of BRCA testing in ovarian FFPE tissue reaches 99% accuracy when NGS validation uses quality control metrics which achieve depth measurements above 40x to decrease false positive results.
Menon & Brash, 2023	*Mutation Research Reviews*	This study reviews NGS QC for low-frequency mutations by evaluating the required depth at >1000x and control implementation which helps identify rare ovarian cancer variants.
McDevitt et al., 2024	*European Journal of Human Genetics*	The guidelines of EMQN recommend strict adoption of the principles of ISO 15189 and also involvement in EQA programmes in combination with specific paired testing in ovarian cancer to obtain high analytical sensitivity.

Table 1 provides a summary of author(s), journal, key findings, validations of 99% (NGS), 95% (multigene panels), and 98% (WGS) sensitivity, requires standardisation, and QC 10% low level of detection. Research recommends the use of EQA, ISO 15189, EMQN, and MIQE guidelines to enhance reliability in the detection of rare alleles and hereditary ovarian cancer variants.

Frequency of Quality Control Measures in Almaty, Kazakhstan

Out of five major QC measures, 17 respondents (68%), and 8 (32%), used positive and negative controls

on a daily and weekly basis, respectively. In 13 cases (52%), DNA quality checks were made on a daily basis, whereas on a weekly basis, it was done in 12 cases (48%). Calibration of equipment was done either once a week or once a month (11% and 44 %, respectively), but there was no mention of equipment being calibrated on a daily basis. In 4 cases (16%), the replicate testing was monthly. These trends suggest that there is high use of daily control to detect an error, however, in calibration may be a weakness as displayed in Table 3 below.

Table 3. Frequency of Key Quality Control Practices

QC Practice	Daily n (%)	Weekly n (%)	Monthly n (%)	Rarely/Never n (%)
Positive/Negative Controls	17 (68)	8 (32)	0	0
DNA Quality Checks	13 (52)	12 (48)	0	0
Equipment Calibration	0	11 (44)	11 (44)	3 (12)
Replicate Testing	0	0	4 (16)	21 (84)

SOP Adherence and IQC Effectiveness

The 15 participants (60 %) reported Full SOP adherence, the 8 participants (32 %) reported partial adherence, and the 2 participants (8 percent) reported no adherence at all. The effectiveness rates of IQC were partly effective (9, 36%), very effective (7, 28%), neutral (5, 20%), partly ineffective (3, 12%), and very inefficient (1, 4%). In general, 64% said they had confidence in IQC, but 16% voiced their concerns. Table 4 below shows the SOP Adherence and IQC Effectiveness.

Table 4. SOP Adherence and IQC Effectiveness

Aspect	Category	n (%)
SOP Adherence	Full	15 (60)
	Partial	8 (32)
	None	2 (8)
IQC Effectiveness	Very effective	7 (28)
	Somewhat effective	9 (36)
	Neutral	5 (20)
	Ineffective	4 (16)

Participation in External Quality Assessment (EQA) Programs

Seventy-six percent (19 respondents) participated in EQA: CAP only (9, 36%), EMQN only (5, 20%), both (5, 20%). Six (24%) reported no participation.

Challenges Faced in Quality Control

Table 5 below highlights the challenges; its impacts and resources deficiencies encountered among laboratory personnels. The main challenges were sample integrity (14, 56%), reagent variability, and staff training (12 each, 48%), equipment problems (10, 40%), and meeting standards (4, 16%). The frequency of challenge impact was sometimes (44%), rarely (28%), or frequently (28%). The important resource gaps highlighted funding (17, 68%), technology (14, 56%), personnel (13, 52%), and time (4, 16%).

Table 5. Major Challenges and Resource Deficiencies

Category	Challenge/Resource Gap	n (%)
Challenges	Sample integrity	14 (56)
	Reagent variability	12 (48)
	Staff training	12 (48)
	Equipment issues	10 (40)
Resource Deficiencies	Funding	17 (68)
	Technology/Equipment	14 (56)
	Personnel	13 (52)
	Time	4 (16)

Staff Recommendations

Among the respondents, better training was proposed by 13 (52%), automation by 9 (36%), sample handling by 8 (32%), more frequent calibration and more controls by 6 each (24%), and better adherence by 3 (12%). Funding (11, 44%), technology/equipment (9, 36%), personnel (7, 28%), software (3, 12%), and time (2, 8%), were the resources required. This can be seen in Table 6 below.

Table 6. Staff Recommendations for QC Improvement and Required Resources

Category	Recommendation / Resource Need	n (%)
Improvement Strategies	Better staff training	13 (52)
	Automation of processes	9 (36)
	Improved sample handling	8 (32)
	More frequent calibration & controls	6 (24)
	Better SOP adherence	3 (12)
Required Resources	Increased funding	11 (44)
	Better technology/equipment	9 (36)
	Additional personnel	7 (28)
	Improved software	3 (12)
	More time allocated	2 (8)

Discussion

The present study evaluated the quality control (QC) procedures in the molecular genetics laboratories conducting diagnostics for ovarian cancer in a resource-limited settings in Kazakhstan. The results showed a mixed picture, with good levels of routine use of positive and negative controls, but some deficiencies in equipment calibration frequency, replicate testing and sample integrity.

When compared with existing literature, the strong emphasis on positive and negative controls is consistent with ISO 15189 recommendations and practices reported in other LMIC settings [14,31]. The equipment calibration and limited replicate testing that were identified in this study does not align with international best practices, as greater testing frequency and more intensive controls are linked to higher accuracy in BRCA1/2 detection [23,25,26]. Similarly, the level of adherence to SOP and perceived effectiveness of internal quality control is deemed moderate, which indicates some regular symptoms in resource-limited settings [13,18].

The involvement in external quality assessment (EQA) programmes was relatively high (76 %), which is encouraging and similar to some high-income settings [28]. However, the rate of non-participation of 24% is problematic, as regular inclusion in EQA has been found to minimise systematic errors in molecular diagnostics [30-33].

The major challenges reported including sample integrity, reagent variability, staff training, and funding shortages are consistent with those documented across low- and middle-income countries [18,24]. These systemic barriers likely contribute to the gaps observed and underscore the difficulties of maintaining high-quality molecular testing for ovarian cancer in resource-limited contexts.

This study contributes to the literature by providing empirical evidence on QC practices in molecular genetics laboratories in Central Asia, a region with limited prior data. The results reflect the achievements in Kazakhstan, but also identify the issues that need to be addressed to improve diagnostic reliability in comparable resource-restricted environments.

Limitations of the Study

There are a number of limitations that this study has and which are to be taken into account when interpreting the results. The small sample size and the concentration on laboratories in one city might be a limitation to the generalizability of the findings to other areas compared to the work of wheeler et al 2023 who conducted a global survey. Moreover, the use of self-reported data presents the risk of reporting bias, in particular, in SOP adherence and QC practices. Even though the systematic review component involved the use of high-quality studies, the disparity in the resource availability across settings may limit any direct comparisons. Irrespective of these shortcomings, the research offers useful baseline information on QC practices in molecular diagnostics in Kazakhstan.

Conclusion

Laboratories of molecular genetics in Almaty, Kazakhstan, have been established with a functioning QC foundation that is characterised by routine control use, reasonable SOP compliance, and meaningful EQA involvement. These strengths enable the reliability of ovarian cancer diagnostics and are in line with national objectives of early cancer detection and better patient outcomes. There are still critical gaps, however, especially regarding the frequency of equipment calibration, the quality of the samples, access to

resources, and lack of regional EQA program which in turn impact the validity of the clinically significant mutation detection, including BRCA1/2. Scalable improvements in practice, better training of the staff, gradual automation, better management of the samples, and increased access to EQA offer viable alternatives to strengthen QC systems within the available resources. Future studies should focus on multi-centre research and the study of cost-effective QC interventions that can be used on a scale to promote precision medicine and reduce the burden of ovarian cancer in LMICs.

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