https://doi.org/10.35845/kmuj.2025.23646

SCOPING REVIEW

MicroRNAs as biomarkers in prostate cancer: a scoping review with implications for the Pakistani healthcare setting

Shameen Fatima Shoaib [1], Maham Javed [1], Maham Akhlaq [1,2], Fazal Ur Rehman Khan Niazi [3], Nadia Naseem [1]

1: Department of Histopathology, University of Health Sciences, Lahore, Pakistan
2: Department of Pathology, Postgraduate Medical Institute Lahore General Hospital, Lahore, Pakistan
3: Department of Urology, Federal Postgraduate Medical Institute National Institute of Kidney Diseases, Shaikh Zayed Hospital Lahore, Pakistan

Email: mahamjaved77@gmail.com
Contact #: +92-345-4507011

Date Submitted: March 25, 2024
Date Revised: December 17, 2025
Date Accepted: December 17, 2025

ABSTRACT

Objective: To critically evaluate the diagnostic, prognostic, and therapeutic significance of microRNAs (miRNAs) in prostate cancer (PCa), with particular emphasis on their potential relevance to the Pakistani healthcare context.

Methods: This scoping review was conducted in accordance with PRISMA-ScR guidelines. Electronic searches were performed in PubMed, MEDLINE, EMBASE, and the Cochrane Library for studies published between January 2010 to June 2025. Regional literature was identified through the Journal of Pakistan Medical Association, Journal of the College of Physicians and Surgeons Pakistan, Pakistan Journal of Medical Sciences, Pakistan Journal of Pathology, and Pakistan Armed Forces Medical Journal. Keywords included microRNA, prostate cancer, diagnostic biomarker and therapeutic target. Original human studies evaluating miRNA expression in prostate cancer tissues or biological fluids with diagnostic, prognostic, or therapeutic implications were included. Reviews, conference abstracts, non-human studies, and studies lacking specific miRNA outcome data were excluded.

Results: Out of 64 identified records, 16 studies met the inclusion criteria. miR-375 and miR-141 emerged as the most consistently dysregulated miRNAs with strong diagnostic potential, frequently incorporated into multi-miRNA panels outperforming prostate-specific antigen alone. Additional miRNAs, including miR-182, miR-200b, miR-21, miR-106b, and miR-1255b-5p, were predominantly upregulated and associated with disease presence, progression, and aggressive pathological features. miR-93 demonstrated post-treatment downregulation, indicating its potential role as a biomarker of therapeutic response.

Conclusion: Current evidence supports the promising role of miRNAs as non-invasive biomarkers for prostate cancer diagnosis, prognosis, and treatment monitoring. However, locally generated data remain scarce, highlighting the need for well-designed Pakistani studies to enable clinical translation.

Keywords: Prostate Cancer (MeSH); MicroRNA (MeSH); Diagnosis (MeSH); Biomarkers (MeSH); Biomarkers, Tumor (MeSH); Therapeutics (MeSH); Therapeutic Uses (MeSH); Prognostic Marker (MeSH); Pakistan (MeSH).

THIS ARTICLE MAY BE CITED AS: Shoaib SF, Javed M, Akhlaq M, Niazi FURK, Naseem N. MicroRNAs as biomarkers in prostate cancer: a scoping review with implications for the Pakistani healthcare setting. Khyber Med Univ J 2025;17(4):493-500. https://doi.org/10.35845/kmuj.2025.23646

INTRODUCTION

Prostate cancer is a health risk that impacts men worldwide and has garnered attention due to its increasing incidence. It stands as the second most prevalent cancer in males on a global scale and ranks as the fifth leading cause of mortality worldwide.[1] The malignancy is preventable through timely screening methods like PSA and TRDE however they are reported to lack sensitivity and specificity. In Pakistan, prostate cancer ranks as the third most frequently diagnosed malignancy in males.[2]

The most common disorders of prostate among aging males are prostatitis and benign prostatic hyperplasia (BPH) which is the nonmalignant enlargement of the prostate. The incidence of BPH increases with age, showing 50% increased incidence rate at 60 years and almost 90% at 80 years of age.[3] Diagnosis of prostate cancer (PCa) is established on prostate biopsy that is performed when the patient has persistently raised (PSA) and an abnormal digital rectal examination (DRE).[4] However, these tests are reported to lack sensitivity and specificity. In patients with PCa undergoing radical prostatectomy (RP), histopathological grade, preoperative (PSA) level, and pathologic stage are considered to be the most important predictors of outcome and prognosis.[5] Gleason pattern is the most dependable and reproducible grading system used throughout the world. Primary and secondary grade patterns are added to calculate the Gleason score, which predicts prognosis and help guide the therapy.[6] Lesser resemblance of the adenocarcinoma to the normal glandular formation defines a higher Gleason grade.[7] PSA levels in many prostate adenocarcinoma patients may not be truly reflective of the malignancy as these levels tend to be higher even in different benign conditions like prostatitis, urinary tract infection and benign prostatic hyperplasia.[8] Therefore, the need of the hour is to discover a biomarker which can aid or may substitute PSA levels for early diagnosis and prognostic determination of prostatic carcinoma.[9]

Recent advancements in medical field have led to the discovery of microRNA. MicroRNA are short, single-stranded non-coding ribonucleic acids (RNAs) typically ranging from 18-22 nucleotides in length,[10] that direct gene expression through the complementary binding to target mRNAs, leading to their degradation.[11] MiRNA expression tends to be more tissue specific, therefore aiding to classify origin of human cancer. In tumorigenesis, miRNAs are abnormally expressed which can either

activate oncogenes or inactivate tumor suppressor genes, leading to tumor formation.[12] MicroRNA expression profiles can be used for the early detection and prognostic markers for different cancers.[13] Previous literature has shown variable expression of different microRNAs in breast, colorectal, ovarian and in prostate cancer.[14] Up or down regulation of a spectrum of miRNAs has been reported in serum of patients with prostatic carcinoma.[15] Over expression of certain miRNA has been consistently reported in PCa in the published literature as compared to the benign prostatic lesions which may depict their potential as diagnostic biomarkers for PCa.[16] In prostate cancer development and progression, the regulation of microRNA is important because these miRNAs tend to target major oncongenes and tumor suppressor genes such as Bcl-2, PTEN, hormonal receptors e.g., androgen receptor (AR) and others.[17] In prostate cancer, different circulating microRNAs have been shown to have diagnostic, predictive, and prognostic capabilities.[18] Overexpressed miRNAs referred as 'oncogenic miRNAs' have the potential to exert negative regulatory effects on tumor suppressor genes (Figure 1).[19] The microRNAs most frequently overexpressed in prostate cancer are miRNA-21, miRNA-32, miRNA-221, miRNA-222, miRNA-181, miRNA-18a, and miRNA-429.[20]

METHODS

This scoping review adhered to the PRISMA-ScR guidelines. Searches were conducted in PubMed, MEDLINE, EMBASE, and Cochrane Library for studies published from 2010 to 2025. Regional searches included Journal of Pakistan Medical Association (JPMA), Journal of the College of Physicians and Surgeons Pakistan (JCPSP), Pakistan Journal of Medical Sciences (PJMS), Pakistan Journal of Pathology, and Pakistan Armed Forces Medical Journal (PAFMJ). The following terms were used in combination of microRNA, miRNA, prostate cancer, diagnostic biomarker, therapeutic target, serum, urine, and Pakistan.

Inclusion Criteria: Included original studies on human subjects investigating miRNA expression in PCa tissues or biological fluids and Studies examining diagnostic, prognostic, or therapeutic implications.

Exclusion criteria: Included Review articles, conference abstracts, or non-human studies and studies without specific miRNA expression data or outcomes.

Data extraction and synthesis: Information that was extracted included the author, year, country, study design, sample size, investigated miRNAs, and their diagnostic or prognostic significance (Table II). Figure I illustrates the PRISMA-ScR flow diagram depicting the study selection process. A total of 64 records were identified through database and regional journal searches. After title and abstract screening, 24 full-text articles were assessed for eligibility. Following exclusion based on predefined criteria, 16 studies were included in the final scoping review.

RESULTS

miR-375 and Its diagnostic role: Multiple studies consistently identified dysregulation of miR-375 in prostate cancer. Bidarra D, et al.,[21] reported

Table I: Table summarizing expression trends (upregulated/downregulated miRNAs)

microRNA	Expression Trend in Prostate Cancer	Associated Findings / Diagnostic Role	Study Source
miR-375 / miR-375-3p	Upregulated	Elevated in advanced pathological stages; diagnostic potential; part of biomarker panels	Bidarra D, et al.,[21]; Jin W, et al.,[22]; Porzycki P, et al.,[24]; Liu RS, et al.,[23]
miR-182 / miR-182-5p	Upregulated	Increased in advanced stages; associated with tumor progression	Bidarra D, et al.,[21]; Jin W, et al.,[22]
miR-141 / miR-141-3p	Upregulated	Strong diagnostic significance; elevated in serum; part of biomarker panels	Jin W, et al.,[22]; Porzycki P, et al.,[24]
miR-200b	Upregulated	Higher in PCa patients; contributes to diagnostic accuracy	Jin W, et al.,[22]
miR-106b	Upregulated	Elevated in PCa group; included in diagnostic panels	Porzycki P, et al.,[24]
miR-21	Upregulated	Elevated serum levels; possible early detection marker	Porzycki P, et al.,[24]
miR-1255b-5p	Upregulated	Strong diagnostic and therapeutic potential	Zhao Y, et al., [25]
miR-223	Upregulated	Part of 3-miRNA panel with high NPV when combined with PSA	Liu RS, et al.,[23]
miR-24	Upregulated	Included in PSA-combined biomarker panel	Liu RS, et al.,[23]
miR-93	Downregulated after treatment	Decrease post-therapy; biomarker for treatment response	Zedan AH, et al., [26]

Table II: Comparison of different studies depicting role of microRNAs conducted over the years (2018-2025)

Author	Title	Place of Study	Year of publication	Study design	Sample size	Conclusion
Singh S, et al.,[27]	Integrating miRNA profiling and machine learning for improved prostate cancer diagnosis	India	2025	prospective cohort study	51 PCa patients and 35 BPH patients	miRNAs such as miR-21-5p, miR-141-3p, and miR-221-3p were identified as significant discriminators between PCa and BPH through a prospective cohort study.
Goztepe M, et al.,[28]	Research of the unrecognised functions of miR-375 in prostate cancer cells	Turkey	2024	Cell culture study	RWPE-1 normal human prostate epithelial cells, AR-sensitive LNCaP prostate cancer cells, AR-insensitive DU-145 and PC-3 prostate cancer cells were recruited for this study.	miR-375 has anti-proliferative and cell migration inhibitory effects in prostate cancer.
Chen M, et al.,[29]	An integrated ceRNA network identifies miR-375 as an upregulated miRNA playing a tumor suppressive role in aggressive prostate cancer	China	2024	Integrated multi-methodological study(Cell culture study)	24	miR-375 predominantly targets genes possessing oncogenic roles (e.g., proliferation, DNA repair, and metastasis), and thus release targets with tumor suppressive functions. This action model well clarifies why an upregulated miRNA plays a tumor suppressive role in PCa.
Gan J, et al.,[30]	MicroRNA-375 is a therapeutic target for castration-resistant prostate cancer through the PTPN4/STAT3 axis	China	2022	Basic and Translational Research	30 PCa and 17 benign prostate hyperplasia tissues	MiR-375 expression was aberrantly increased in PCa tissues and cancer exosomes, correlating with the Gleason score. targeting miR-375 may be an alternative therapeutic for PCa, especially for CRPC with high AR levels.
Zhao Y, et al.,[25]	Diagnostic significance of microRNA-1255b-5p in prostate cancer patients and its effect on cancer cell function	Shanghai	2021	Case control study	103 BPH and 153 prostate cancer patients	MiRNA-1255b-5p promotes prostate cancer cell proliferation, invasion, and migration in vitro, indicating that it may be an onco-miRNA in prostate cancer. Moreover, miR-1255b-5p is a powerful biomarker for prostate cancer diagnosis and may become a potential therapeutic target for prostate cancer.

continued..

Author	Title	Place of Study	Year of publicatio	Study design	Sample size	Conclusion
Hoey C, al.,[31]	Circulating miRNAs as non-invet asive biomarkers to predict aggressive prostate cancer after radical prostatectomy	Canada	2019	Descriptive cross-sectional	78 PCa patients	High expression of four-miRNAs (miR-17, miR-20a, miR-20b, miR-106a) in blood samples is indicative of high-risk disease that is likely to recur after radical prostatectomy. Future studies will reveal the clinical utility of these miRNAs as predictive or prognostic biomarkers.
Bidarra D, et al.,[21]	Circulating MicroRNAs as Biomarkers for Prostate Cancer Detection and Metastasis Development Prediction	Portugal	2019	Prospective cohort study	A total of 98 PCa and 15 normal prostate samples to assess PCa-specificity of miR-182-5p and miR-375-3p in tissues.	High circulating levels of both miR-182-5p and miR-375-3p were associated with more advanced pathological stages. Hence, these two circulating miRNAs might be clinically useful as non-invasive biomarkers for detection and prediction of metastasis development at the diagnosis together with clinical variables used in routine practice.
Zedan AH, et al.,[26]	MicroRNA expression in tumour tissue and plasma in patients with newly diagnosed metastatic prostate cancer	Denmark	2018	Prospective cohort study	1.Tissue samples- 46 2. Plasma samples- 149	MiRNA-93 demonstrated a significant correlation between tumor tissue and plasma samples in a cohort of patients with PCa, and its plasma level decreased significantly after treatment in local/locally advanced PCa patients, supporting its potential as a PCa biomarker. Moreover, the potential tumor suppressive role of let-7b and the oncogenic role of miRNA-21 were well-supported by this study in tumor tissue and plasma.
Porzycki P, et al.,[24]	Combination of three miRNA (miR-141, miR-21, and miR-375) as potential diagnostic tool for prostate cancer recognition	Poland	2018	Case control Study	20 diagnosed PCa patients and 10 healthy controls	The miR-106b, miR-141-3p, miR-21, and miR-375 showed an increased expression level in the PCa group. This study emphasized the use of these serum miRNAs for non-invasive and specific detection of PCa. Moreover, a combination of these miRNAs stand out as promising panel markers with a diagnostic potential.
Liu RS, et al.,[23]	Assessment of Serum microRNA Biomarkers to Predict Reclassification of Prostate Cancer in Patients on Active Surveillance	Canada	2018	Prospective cohort study	196 and 133 diagnose PCa patients with Gleason Score 6	The 3-miR (miRNA-223, miRNA-24 and miRNA-375) score combined with prostate specific antigen represents a noninvasive biomarker panel with high negative predictive value (90%). It may be used to identify patients on active surveillance who have truly indolent prostate cancer.

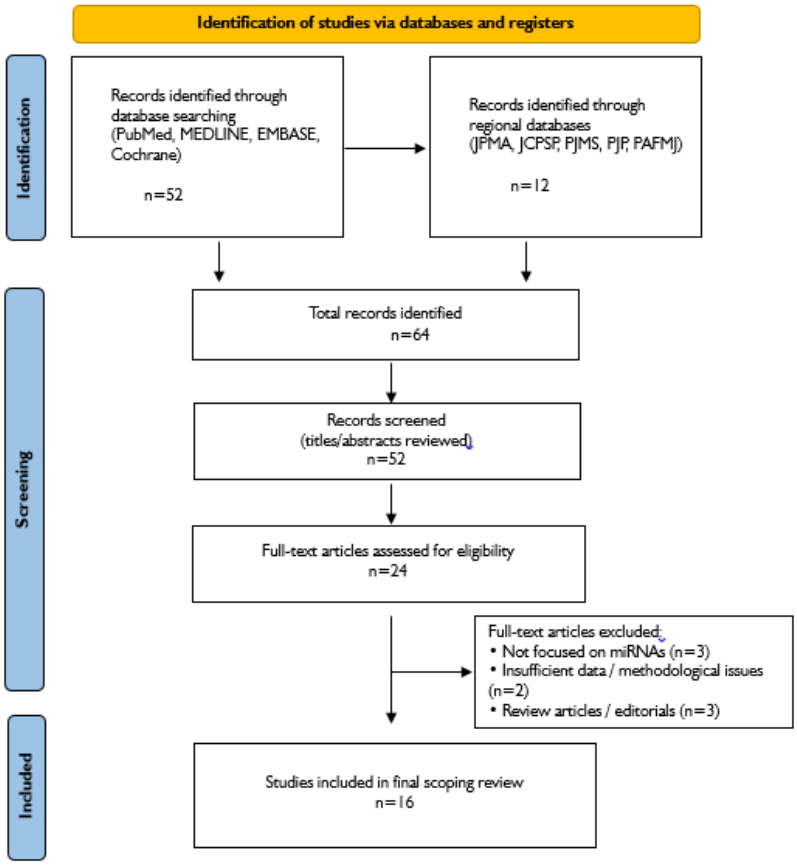

Figure 1: PRISMA flowchart diagram of the study

altered miR-375 expression with strong evidence for its utility as a diagnostic biomarker. They further noted that advanced pathological stages showed elevated levels of miR-182-5p and miR-375-3p, suggesting a role in disease progression. Jin W, et al.[22] found significantly higher serum levels of miR-375, along with miR-141, miR-182, and miR-200b, in prostate cancer patients. Liu RS, et al.,[23] included miR-375 in a three-microRNA panel (miR-223, miR-24, miR-375) combined with PSA that yielded a negative predictive value of ~90%, particularly useful for distinguishing truly non-aggressive cancers under active surveillance.

miR-141 and related diagnostic panels: Several studies highlighted the diagnostic significance of miR-141. Porzycki P, et al.[24] demonstrated that miR-141 has strong diagnostic potential. Their study also showed elevated expression of miR-106b, miR-141-3p, miR-21, and miR-375 in prostate cancer patients. These serum microRNAs collectively showed promise for non-invasive and early detection, especially when used as a combined biomarker panel.

miR-1255b-5p: Another independent study showed miR-1255b-5p to be a powerful diagnostic biomarker with potential as a therapeutic target for prostate cancer.[25]

miR-93 as a biomarker of treatment response: A Danish study by Zedan AH, et al.,[26] reported a significant correlation between miR-93 levels in tumor tissue and matched plasma samples. A marked reduction in plasma miR-93 levels after treatment supports its role as a dynamic biomarker for treatment monitoring.

Table I summarizes dysregulated microRNAs in prostate cancer, highlighting predominantly upregulated miRNAs with diagnostic and prognostic relevance, many of which are incorporated into biomarker panels or show association with advanced disease stages. Additionally, miR-93 demonstrates post-treatment downregulation, suggesting potential utility as a marker of therapeutic response.

DISCUSSION

This review summarizes recent research on the role of microRNAs (miRNAs) in the diagnosis, prognosis, and treatment of prostate cancer. Overall, the findings suggest that several miRNAs have important clinical value, especially in distinguishing prostate cancer from benign prostatic hyperplasia and in identifying aggressive disease.

The collective evidence demonstrates that numerous microRNAs-including miR-375, miR-141, miR-182, miR-200b, miR-93, and miR-1255b-5p hold substantial promise as diagnostic, prognostic, and therapeutic biomarkers in prostate cancer. Their consistent elevation in patient samples and association with pathological stage, tumor aggressiveness, and treatment response suggests that microRNAs may enhance early detection and personalized management strategies.

Multiple independent studies validate recurring patterns of miRNA dysregulation as demonstrated in Table I. Many miRNAs (e.g., miR-375, miR-141) are detectable in serum, supporting non-invasive testing. Combination miRNA panels demonstrate high predictive perf-ormance and complement PSA testing. Certain miRNAs (e.g., miR-93) have the added advantage of tracking treatment response, expanding clinical utility beyond initial diagnosis. MiRNAs also influence androgen receptor (AR) regulation, PI3K/AKT pathway, Apoptosis control. MiR-221/222 modulate AR signaling loops that govern prostate cell proliferation. MiR-21 downregulates PTEN, activating proliferative signaling. MiR-375 affects BCL-2-mediated pathways, influencing therapy resistance.

A major strength across these studies is the use of diverse and complementary study designs, ranging from prospective cohort and case–control studies to basic, translational, and integrated multi-methodological research. This triangulation enhances the biological plausibility and clinical relevance of the findings. Several studies by Bidarra D, et al.,[21] Liu RS, et al.,[23] and Singh M, et al.,[32] employed prospective designs, which

reduce recall bias and better establish temporal associations between miRNA expression and disease outcomes. Additionally, the repeated identification of specific miRNAs most notably miR-375, miR-141, miR-21, and miR-182 across different populations and settings strengthens their credibility as unique biomarkers.

Another notable strength is the shift toward non-invasive diagnostics using circulating miRNAs in serum or plasma. Literature has demonstrated that circulating miRNAs correlate with tumor burden, pathological stage, treatment response, and risk of progression or recurrence. Furthermore, mechanistic studies by Chen J-Y, et al.,[33] Gan J, et al.,[30] and Merve Goztepe M, et al.,[28] provide functional insights, showing that miRNAs such as miR-375 may exert tumor suppressive or context-dependent roles, thereby bridging molecular biology with clinical observations.

Limitations of the study

Despite these strengths, several limitations must be acknowledged. Many studies have relatively small sample sizes, particularly those involving tissue-based analyses or in vitro experiments, which limits statistical power and generalizability. Heterogeneity in study populations, miRNA detection platforms, normalization methods, and outcome measures also complicates direct comparison and meta-analysis. For example, miR-375 is reported as upregulated and tumor suppressive in some studies, while others associate its increased expression with advanced disease and higher Gleason scores, suggesting context-dependent or stage-specific effects.

Additionally, many investigations are observational and cross-sectional validation cohorts are often lacking, and few studies assess long-term clinical endpoints such as overall survival. There is also limited integration of miRNA panels into standardized clinical workflows, and cost-effectiveness analyses are largely absent. Finally, most studies were conducted in single countries or centers, raising concerns about ethnic and geographic variability in miRNA expression profiles. Most data originate from non-Pakistani populations, raising concerns about applicability due to genetic, environmental, and lifestyle variations. Current diagnostic modalities in Pakistan suffer from issues of accessibility, affordability, and limited accuracy.

Clinical implications and future directions: Clinically, these findings support the potential of miRNAs as adjuncts to prostate-specific antigen (PSA) testing, addressing its well-known limitations in specificity. Panels incorporating miRNAs such as miR-375, miR-141, miR-21, and miR-223 show promise in improving diagnostic accuracy, reducing unnecessary biopsies, and aiding risk stratification, particularly in patients on active surveillance. The high negative predictive value reported by Liu RS, et al.,[23] suggests a meaningful role in identifying truly indolent disease.

From a therapeutic perspective, mechanistic studies identifying miRNAs as oncogenic or tumor suppressive regulators (e.g., miR-375 via the PTPN4/STAT3 axis, miR-1255b-5p as an onco-miRNA) open avenues for miRNA-based targeted therapies, especially in castration-resistant prostate cancer. However, clinical translation will require large, multicenter validation studies, standardized assay protocols, and regulatory approval pathways.

There is a strong rationale for conducting Pakistan-specific studies to evaluate regional patterns of miRNA expression. Developing locally validated miRNA biomarker panels could significantly improve diagnostic accuracy, reduce delays in management, and support individualized treatment decisions. Further research should explore not only diagnostic roles but also the therapeutic potential of miRNAs and their integration into targeted treatment strategies.

CONCLUSION

microRNAs demonstrate substantial potential as non-invasive diagnostic, prognostic, and treatment-monitoring biomarkers in prostate cancer, with growing evidence supporting their role in disease stratification and personalized care. Although international studies consistently highlight their clinical relevance, the absence of population-specific validation and standardized methodologies in Pakistan limits their immediate translational application. Future research should prioritize large-scale, well-designed, multicenter studies within the Pakistani population, integrating molecular miRNA profiling with established clinical and pathological parameters. Such efforts are essential to develop reliable, cost-effective, and locally applicable miRNA-based assays, facilitating their eventual incorporation into routine prostate cancer management.

REFERENCES

1. Obafemi F, Umahi-Ottah G. A review of global cancer prevalence and therapy. J Cancer Res Treat Prev 2023;1(3):128-47. https://doi.org/10.37191/Mapsci-JCRTP-1(3)-011
2. Akhtar S, Hassan F, Ahmad S, El-Affendi MA, Khan MI. The prevalence of prostate cancer in Pakistan: a systematic review and meta-analysis. Heliyon 2023;9(10):e20350.https://doi.org/10.1016/j.heliyon.2023.e20350
3. Awedew AF, Han H, Abbasi B, Abbasi-Kangevari M, Ahmed MB, Almidani O, et al. The global, regional, and national burden of benign prostatic hyperplasia in 204 countries and territories from 2000 to 2019: a systematic analysis for the Global Burden of Disease Study 2019. Lancet Healthy Longev 2022;3(11):e754-e76.https://doi.org/10.1016/S2666-7568(22)00213-6
4. Chung Y, Hong SK. Evaluating prostate cancer diagnostic methods: the role and relevance of digital rectal examination in modern era. Investig Clin Urol 2025;66(3):181-7. https://doi.org/10.4111/icu.20240456
5. Di Mauro E, Di Bello F, Califano G, Morra S, Creta M, Celentano G, et al. Incidence and predicting factors of histopathological features at robot-assisted radical

prostatectomy in the mpMRI era: results of a single tertiary referral center. Medicina 2023;59(3):625-39.https://doi.org/10.3390/medicina59030625

6. Zelic R, Giunchi F, Fridfeldt J, Carlsson J, Davidsson S, Lianas L, et al. Prognostic utility of the gleason grading system revisions and histopathological factors beyond gleason grade. Clin Epidemiol 2022:59-70. https://doi.org/10.2147/clep.s339140

7. Godtman RA, Kollberg KS, Pihl C-G, Månsson M, Hugosson J. The association between age, prostate cancer risk, and higher Gleason score in a long-term screening program: results from the Göteborg-1 prostate cancer screening trial. Eur Urol 2022;82(3):311-7. https://doi.org/10.1016/j.eururo.2022.01.018

8. Merriel SWD, Pocock L, Gilbert E, Creavin S, Walter FM, Spencer A, et al. Systematic review and meta-analysis of the diagnostic accuracy of prostate-specific antigen (PSA) for the detection of prostate cancer in symptomatic patients. BMC Med 2022;20(1):54-64. https://doi.org/10.1186/s12916-021-02230-y

9. Van Poppel H, Albreht T, Basu P, Hogenhout R, Collen S, Roobol M. Serum PSA-based early detection of prostate cancer in Europe and globally: past, present and future. Nat Rev Urol 2022;19(9):562-72. https://doi.org/10.1038/s41585-022-00638-6

10. George TP, Subramanian S, Supriya M. A brief review of noncoding RNA. Egypt J Med Hum Genet 2024;25(1):98-103. https://doi.org/10.1186/s43042-024-00553-y

11. Naeli P, Winter T, Hackett AP, Alboushi L, Jafarnejad SM. The intricate balance between microRNA-induced mRNA decay and translational repression. FEBS J 2023;290(10):2508-24. https://doi.org/10.1111/febs.16422

12. Khorkova O, Stahl J, Joji A, Volmar C-H, Wahlestedt C. Amplifying gene expression with RNA-targeted therapeutics. Nat Rev Drug Discov 2023;22(7):539-61. https://doi.org/10.1038/s41573-023-00704-7

13. Zhang C, Sun C, Zhao Y, Wang Q, Guo J, Ye B, et al. Overview of MicroRNAs as diagnostic and prognostic biomarkers for high-incidence cancers in 2021. Int J Mol Sci 2022;23(19):11389. https://doi.org/10.3390/ijms231911389

14. Veryaskina YA, Titov SE, Zhimulev IF. Reference genes for qPCR-based miRNA expression profiling in 14 human tissues. Med Princ Pract 2022;31(4):322-32. https://doi.org/10.1159/000524283

15. Xiang Z, Lin T, Ling J, Xu Z, Huang-R, Hu H. MiRNA expression profiling and clinical implications in prostate cancer across various stages. Sci Rep 2025;15(1):7771-80. https://doi.org/10.1038/s41598-025-92091-9

16. Li W, Xu W, Sun K, Wang F, Wong TW, Kong AN. Identification of novel biomarkers in prostate cancer diagnosis and prognosis. J Biochem Mol Toxicol 2022;36(9):e23137. https://doi.org/10.1002/jbt.23137

17. Sidorova EA, Zhernov YV, Antsupova MA, Khadzhieva KR, Izmailova AA, Kraskevich DA, et al. The role of different types of microRNA in the pathogenesis of breast and prostate cancer. Int J Mol Sci 2023;24(3):1980-96.https://doi.org/10.3390/ijms24031980

18. Samami E, Pourali G, Arabpour M, Fanipakdel A, Shahidsales S, Javadinia SA, et al. The potential diagnostic and prognostic value of circulating MicroRNAs in the assessment of patients with prostate cancer: rational and progress. Front Oncol 2022;11:716831.https://doi.org/10.3389/fonc.2021.71683

19. Lee SH, Ng CX, Wong SR, Chong PP. MiRNAs overexpression and their role in breast cancer: implications for cancer therapeutics. Curr Drug Targets 2023;24(6):484-508. https://doi.org/10.2174/1389450124666230329123409

20. Ghamlouche F, Yehya A, Zeid Y, Fakhereddine H, Fawaz J, Liu Y-N, et al. MicroRNAs as clinical tools for diagnosis, prognosis, and therapy in prostate cancer. Transl Oncol 2023;28:101613.https://doi.org/10.1016/j.tranon.2022.101613

21. Bidarra D, Constâncio V, Barros-Silva D, Ramalho-Carvalho J, Moreira-Barbosa C, Antunes L, et al. Circulating microRNAs as biomarkers for prostate cancer detection and metastasis development prediction. Front Oncol 2019;9:1-8. https://doi.org/10.3389/fonc.2019.00900

22. Jin W, Fei X, Wang X, Chen F, Song Y. Circulating miRNAs as biomarkers for prostate cancer diagnosis in subjects with benign prostatic hyperplasia. J Immunol Res Ther 2020;2020:5873056. https://doi.org/10.1155/2020/5873056

23. Liu RS, Olkhov-Mitsel E, Jeyapala R, Zhao F, Commisso K, Klotz L, et al. Assessment of serum microRNA biomarkers to predict reclassification of prostate cancer in patients on active surveillance. J Urol 2018;199(6):1475-81.https://doi.org/10.1016/j.juro.2017.12.006

24. Porzycki P, Ciszkowicz E, Semik M, Tyrka M. Combination of three miRNA (miR-141, miR-21, and miR-375) as potential diagnostic tool for prostate cancer recognition. Int Urol Nephrol 2018;50(9):1619-26. https://doi.org/10.1007/s11255-018-1938-2

25. Zhao Y, Tang X, Zhao Y, Yu Y, Liu S. Diagnostic significance of microRNA-1255b-5p in prostate cancer patients and its effect on cancer cell function. Bioengineered 2021;12(2):11451-60. https://doi.org/10.1080/21655979.2021.2009413

26. Zedan AH, Hansen TF, Assenholt J, Pleckaitis M, Madsen JS, Osther PJS. microRNA expression in tumour tissue and plasma in patients with newly diagnosed metastatic prostate cancer. Tumour Biol 2018;40(5):1010428318775864.https://doi.org/10.1177/1010428318775864

27. Singh S, Pathak AK, Kural S, Kumar L, Bhardwaj MG, Yadav M, et al. Integrating miRNA profiling and machine learning for improved prostate cancer diagnosis. Sci Rep 2025;15(1):30477-88. https://doi.org/10.1038/s41598-025-99754-7

28. Goztepe M, Eroglu O. Research of the unrecognised functions of miR-375 in prostate cancer cells. Cell Mol Biol 2024;70(3):212-8. https://doi.org/10.14715/cmb/2024.70.3.32

29. Chen M, Zou C, Tian Y, Li W, Li Y, Zhang D. An integrated ceRNA network identifies miR-375 as an upregulated miRNA playing a tumor suppressive role in aggressive prostate cancer. Oncogene 2024;43(21):1594-607. https://doi.org/10.1038/s41388-024-03011-6

30. Gan J, Liu S, Zhang Y, He L, Bai L, Liao R, et al. MicroRNA-375 is a therapeutic target for castration-resistant prostate cancer through the PTPN4/STAT3 axis. Exp Mol Med 2022;54(8):1290-1305. https://doi.org/10.1038/s12276-022-00837-6

31. Hoey C, Ahmed M, Fotouhi Ghiam A, Vesprini D, Huang X, Commisso K, et al. Circulating miRNAs as non-invasive biomarkers to predict aggressive prostate cancer after radical prostatectomy. J Transl Med 2019;17(1):173-83.https://doi.org/10.1186/s12967-019-1920-5

32. Singh M, Jha R, Melamed J, Shapiro E, Hayward SW, Lee P. Stromal androgen receptor in prostate development and cancer. Am J Pathol 2014;184(10):2598-607.https://doi.org/10.1016/j.ajpath.2014.06.022

33. Chen J-Y, Wang P-Y, Liu M-Z, Lyu F, Ma M-W, Ren X-Y, et al. Biomarkers for prostate cancer: from diagnosis to treatment. Diagnostics 2023;13(21):3350.https://doi.org/10.3390/diagnostics13213350

AUTHORS' CONTRIBUTION

The Following authors have made substantial contributions to the manuscript as under:

SFS: Study design, analysis and interpretation of data, drafting the manuscript, critical review, approval of the final version to be published

MJ: Conception, acquisition,analysis and interpretation of data, drafting the manuscript, approval of the final version to be published

MA & FURKN: Acquisition, analysis and interpretation of data, critical review, approval of the final version to be published

NN: Study design, critical review, approval of the final version to be published

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

CONFLICT OF INTEREST

Authors declared no conflict of interest, whether financial or otherwise, that could influence the integrity, objectivity, or validity of their research work.

GRANT SUPPORT AND FINANCIAL DISCLOSURE

Authors declared no specific grant for this research from any funding agency in the public, commercial or non-profit sectors

DATA SHARING STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request

KMUJ web address: www.kmuj.kmu.edu.pk
Email address: kmuj@kmu.edu.pk