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Cervical cancer screening: a comparative study of TruScreen vs. Pap Smear

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Abstract

Objectives This study aimed to evaluate the potential of real-time optoelectronic device (TruScreen™; TS; TruScreen Group Limited, New Zealand) as an alternative or adjunct to Pap Smear (Liquid Based Cytology (LBC)) for cervical cancer screening.

Method We conducted a prospective observational pilot study involving 507 women who were routinely followed at gynecology clinics. All participants underwent TS and LBC examinations after study enrolment. Those with abnormal findings were referred for colposcopy and cervical biopsy within one month.

Results Overall, 507 women fulfilled the eligibility criteria and were included in this study, of which 30 women (5.9%) had abnormal TS findings and underwent colposcopy. Thirteen women (43.3%) had low-grade lesions, and only one (3.3%) had a high-grade lesion. Regarding biopsy findings, three women had cervical intraepithelial neoplasia (CIN) 1, two women had 'CIN2 + , and one had glandular hyperplasia. The TS yielded a sensitivity of 83.3% (95% CI: 35.9–99.6%) and a specificity of 95% (95% CI: 92.7- 96.8%) for the detection of cervical abnormality, compared to 66.7% (95% CI: 22.3–95.7%) and 98.2% (95%: CI 96.6%-99.2%) of the Pap smear, respectively. The difference between both screening tools was not statistically significant (p = 0.91). The sensitivity (100%, 95% CI 15.6–100%) and specificity (95.6%, 95% CI 93.4–97.2%) of TS and Pap smear for 'CIN2 + lesions were notably high.

Conclusion TS demonstrated potential as a screening tool for cervical neoplasms in this preliminary study. The tool did not require cervical samples, laboratory equipment, or highly trained personnel. While our findings suggest the potential for real-time and accurate screening, further research with a larger sample size is necessary to confirm its reliability and practicality.

Keywords Cervical cancer, Optoelectronic cervical screening, TruScreen, Real-time screening, Optoelectronic device, Pap smear, CIN

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Introduction

Worldwide, cervical cancer ranks as the fourth most common cancer and cause of cancer-related mortality among women [1]. According to the Global Cancer Statistics (GLOBOCAN 2020) report, there were about 604,000 females diagnosed with cervical cancer, with an estimated mortality rate of 342,000 women in 2020 [2]. The incidence and death rates of cervical cancer were profoundly elevated (about 85%) in low to middle-income countries, while they accounted for only 3.6% of new cancers in developed countries [3]. This increased incidence and mortality rates correlate significantly with the lack of screening programs for cervical cancer [4, 5].

Human papillomavirus (HPV) infection is a major risk factor for cervical cancer, as the infection can lead to cervical intraepithelial neoplasia (CIN) [6]. Nonetheless, it takes about 5–10 years for lesions to progress from 'CIN2 +to invasive cancer [7]. Therefore, cervical cancer is considered a preventable malignancy, and there is a great opportunity for early detection of the precancerous lesion by screening methods [8, 9].

In light of this, the World Health Organization (WHO) has aimed to eliminate cervical cancer by 2030 through a comprehensive approach that includes prevention, early diagnosis, effective screening, and treatment programs [10]. Cervical cancer prevention is critical for lowering the disease burden and achieving sustainable development goals for health [11]. Moreover, multiple vaccines are available to protect against common cancer-causing types of HPV [12].

Furthermore, early diagnosis is also critical for reducing the incidence and mortality of cervical cancer, yet many countries, including Saudi Arabia, have no established national screening programs. In women with pathologically detected lesions, cryotherapy or loop electrosurgical excision procedure (LEEP) are effective excisional techniques. To prevent cancer development or treat it at an early stage, the WHO recommends the following screening modalities: HPV, cytology, and visual inspection with acetic acid (VIA) for women whose transformation zone is visible [5].

Over the last few decades, the importance of national screening programs for detecting the early stages of cervical cancer has emerged. The Pap smear, i.e., conventional cytology, is the most commonly used test; however, it has limitations regarding sensitivity and specificity. The false negative rate has been reported to be as high as 53%, which is related to subjective errors in smear preparation and evaluation [5, 13]. Besides, the cytology results cannot be obtained promptly, increasing the risk of women being lost to follow-up. In many countries, including Saudi Arabia, two visits are required to obtain the results of cytology screening within one to two weeks.

Colposcopic assessment following abnormal cytological changes is a diagnostic tool that has more accuracy than traditional cytology and an estimated overall sensitivity and specificity of 80% and 92%, respectively [9, 14]. Colposcopy is considered a cost-effective diagnostic paradigm, especially in poor-resource settings. However, visual experience and well-trained healthcare professionals are required to evaluate the results accurately [15–17]. With the evolution of scientific technology, a novel real-time optoelectronic device called TruScreen (TS) has been introduced. It is considered to be an expert system approach using artificial intelligence. It has substantial advantages, being a highly objective, non-invasive, simple, and self-checking tool with real-time results and minimal resource costs [5, 18]. Several studies have proven the clinical validation of the TS device [5, 19–21], and a multicentre investigation looked at the screening utility of the TS and Pap smear combination [22]. It showed that the combination improved the sensitivity for CIN 3+ diagnosis from 69 to 93% [22].

The burden of cervical cancer is still considerable in the Middle East region despite the implementation of several screening programs in the region. Despite several reports of the use of TS for cervical cancer screening over the past few years, there have been very few from the Middle East. Therefore, this study aimed to determine whether the real-time optoelectronic device (TruScreen™) could be used as an alternative or adjunct to Pap Smear (Liquid Based Cytology) for cervical cancer screening.

Patients and methods

The report of the present study was prepared in concordance with the statement of the Standards for Reporting Diagnostic Accuracy (STARD) [23]. The study was conducted in accordance with the Declaration of Helsinki, and the protocol was approved by the Ethics Committee of the institutional review board (IRB) (Ref No. Dr. Sulaiman Al-Habib Medical Group – RC20.08.91- Aug 2020). All patients were required to sign the informed consent before enrolment.

Study design and subjects

We conducted a prospective observational pilot multicentre study that recruited women who were routinely followed at the gynecology clinics of Arrayan, Olaya and Takhassusi hospitals of Al-Habib Medical Group, Riyadh, Saudi Arabia, from January 2021 to January 2022. The study invited five hundred and ninety-one women aged 23–65 who presented consecutively at the outpatient gynaecology clinics during data collection. All reproductive age group women who attended the outpatient gynaecology clinics during the study period were eligible for the study. The inclusion criteria

included the agreement to participate in the study and signing the informed consent, with no previous history of hysterectomy, and not menstruating, pregnant, or post-partum. Conversely, women who had a confirmed diagnosis of carcinoma or had any vaginal infection were excluded from the study.

All eligible women underwent opportunistic TS and Pap smear examinations by gynecologists (who had proper training on TS) after enrolment. Women with abnormal findings were referred for colposcopy and cervical biopsy within one month. Before the examination, the following data were collected: age, ethnicity, smoking status, obstetric history, presence of any inter-menstrual bleeding, human immunodeficiency virus (HIV) status, history of HPV or warts, immunosuppressant use, method of contraception, HPV vaccination status and previous Pap smear history.

TruScreen and Pap Smear examinations

The TS examination was performed using TruScreen Pty Ltd (NZX/ASX: TRU) with the woman in the lithotomy position. The device provided a real-time cervical assessment following the application of the disposable photoelectric sensor to ≥ 15 cervical epithelial sites.

The TruScreen device is a real-time optoelectronic screening tool that detects precancerous and cancerous cervical lesions by comparing the optical and electrical physical characteristics and behaviors of the tissue of interest with those of known tissue types.

The device comprises a handheld probe connected to a wireless electromagnetic induction Qi charging cradle, with a total length of approximately 37 cm from base to tip (Figs. 1, 2 and 3). The length of the part of the probe that is inserted into the vagina is 120 mm, and the diameter of its tip is approximately 5 mm. The handpiece probe is also covered by a sheath that incorporates a single-use

Fig. 1 TruScreen ultra handheld device

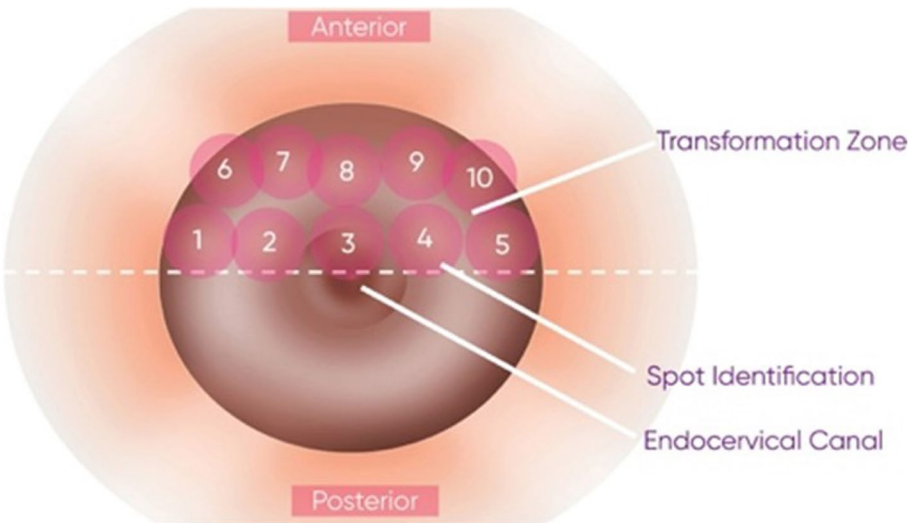

Fig. 2 Images of the Probing Pattern as Shown in the TruScreen Instruction Manual. *Begin probing the outer area of the ectocervix at Spot 1 on the left-hand side and move horizontally from left to right. Complete two rows, to ensure covering the entire anterior part of the ectocervix*

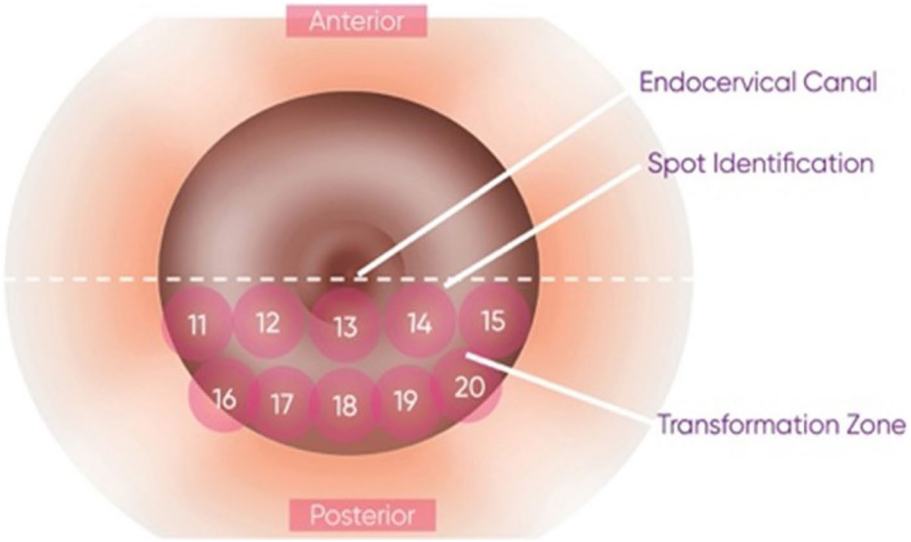

Fig. 3 The Posterior Part of the Ectocervix. It should proceed horizontally from left to right as depicted above

sensor (SUS), increasing the tip diameter to about 6.5 mm. The SUS is a single-use element that ensures sterility, minimizes cross-contamination, and improves measurement consistency for reliable screening results.

The device classified all results as either normal or abnormal. All operators were blinded to the results of any previous Pap smears, and the examination was performed without colposcopic visualization. Likewise, the laboratory technicians were blinded to the results of TS. The Pap smear examination was conducted using the Liquid Based Cytology, and the results were interpreted according to the Bethesda system 2001 [24]. The TS and Pap smear were performed at the same session.

Colposcopy and biopsy

Women with abnormal TS or Pap smear results were referred for colposcopic examination by a qualified gynecologist. Biopsies were obtained from abnormal areas and sent for histopathology. Patients whose squamocolumnar junction could not be fully exposed had an endocervical curettage. Patient management was based on a 2-tier grading system for low-grade (CIN 1) and high-grade ('CIN2 + and CIN 3 +) abnormalities [25].

Statistical analysis

The sample size was calculated to detect a significant sensitivity, given that the prevalence of CIN 2 + ranges between 5 and 20% in a referral hospital. Based on these prevalence rates and a 95% confidence interval (95% CI), a sample size of 600 patients was a conservative estimate for the study covering most gynecological abnormalities. The selected patients for the clinical performance evaluation have a higher prevalence of abnormal lesions compared to the general population, which allows for the assessment of the sensitivity and the false negative rate of the device. A loss of follow-up up to 20% was also considered.

The statistical analysis was conducted using Stata version 16.0 *(Stata Corp LLC, College Station, TX 77845, USA)*. Data were summarized using mean and standard deviation (SD) for continuous parameters, while counts and percentages were used for categorical parameters. The screening performance of TS and Pap smear was calculated with a 95% CI using sensitivity (number of patients with pathologically diagnosed lesions who had abnormal results divided by all patients with pathologically diagnosed lesions X 100), specificity (number of patients with normal results divided by all patients with normal pathologies X 100), positive predictive value (PPV; the number of patients with true positive results divided by the number of patients with true positive and false positive results X 100), and negative predictive value (NPV; the number of patients with true negative results divided by the total number of patients with negative results X 100). The Chi-square test or Fisher's exact test was used to compare the screening performance of TruScreen (TS) and Pap smear, as appropriate. A *P*-value of less than 0.05 was considered statistically significant.

Results

A total of 601 patients were recruited, with 94 women excluded. 24 lost follow-ups, and 70 had one of the tests or both positive but didn't undergo colposcopy and biopsy for confirmation of the abnormality because of

unavailable resources. 507 women fulfilled the eligibility criteria and were included, with a mean age of 38.7 ± 8.5 years (range 23–61). Most women were Arabs (79.3%), and only (4.7%) were smokers. Overall, 22.5% and 12.6% of the women reported a history of abnormal vaginal and post-coital bleeding, respectively. Seventy-nine women (15.6%) were on one or more contraceptive methods, mainly combined oral contraceptives. Only one woman (0.2%) had HIV, while 16 women (3.2%) had a history of HPV/vaginal warts. Nearly 27% of the women reported previous Pap smear results, and 18.7% of them were abnormal (Table 1).

Findings TruScreen, Pap Smear, Colposcopy, and Biopsy

Overall, 30 women (5.9%) had abnormal TS findings. The distribution of Pap smear results was as follows: 97.2% were negative for intraepithelial lesion or malignancy (NILM), 1.8% were abnormal (0.6% ASC-US, 0.8% LSIL, 0.4% HSIL), and 1.2% yielded unsatisfactory samples. When we correlated the findings of TS with Pap smear results, we observed the following: 14 women with normal smear results had an abnormal TS (2.8%); two of the three women with ASC-US (66.7%) and two of the four women with LSIL (50%) had a normal TS, and none of the patients with endometrial cells had an abnormal TS (Fig. 4). Thirty women underwent colposcopy, of whom 13 (43.3%) had low-grade colposcopic impressions, and only one (3.3%) had a high-grade colposcopic impression. Nine women (30%) had vascular patterns, while none of the women had microinvasion (Fig. 5). Regarding biopsy findings, three women had CIN 1, two had CIN 2 +, and one had glandular hyperplasia.

Screening Performance of TruScreen and Pap Smear

The TS yielded a sensitivity of 83.3% (95% CI: 35.9%—99.6%) and a specificity of 95% (95% CI: 92.7%—96.8%) for the detection of pathologically diagnosed cervical neoplasms, compared to 66.7% (95% CI: 22.3%—95.7%) and 98.2% (95% CI: 96.6%—99.2%) for Pap smear, respectively. The difference between both screening tools was not statistically significant (p = 0.91). For women with CIN 1, the TS had a sensitivity of 66.7% (95% CI: 12.5% – 98%) and a specificity of 95.6% (95% CI: 93.4%—97.2%), compared to 66.7% (95% CI: 12.5% – 98%) and 98.2%

Table 1 Demographics and baseline characteristics of the included women

Variables		Women (*n* = 507)
Age (Year), mean ± SD		38.7 ± 8.5
Ethnicity, N (%)	Arab	402 (79.3)
	Indian	16 (3.1)
	Asian	57 (11.2)
	African	2 (0.4)
	Caucasian	11 (2.2)
	Other	19 (3.7)
Smoking, N (%)		24 (4.7)
Parity, mean ± SD		2.7 ± 1.9
Abnormal vaginal bleeding, N (%)		114 (22.5)
Postcoital bleeding, N (%)		73 (14.4)
Contraception, N (%)		79 (15.6)
Contraception type, N (%)	Combined contraceptives	42 (8.3)
	IUCD	30 (5.9)
	IMPLANON/DEPO/pop	6 (1.2)
Known HIV, N (%)		1 (0.2)
HPV/vaginal warts, N (%)		16 (3.2)
Immunosuppressant use, N (%)		7 (1.4)
HPV vaccination, N (%)		6 (1.2)
Previous Smear, N (%)		136 (26.8)
Smear Results*, N (%)	Normal	106 (77.9)
	Abnormal	25 (18.7)
	Unsatisfactory	1 (0.7)
Previous HPV test, N (%)		9 (1.8)

Abbreviations: IUCD, Intrauterine contraceptive device, *HIV* Human Immunodeficiency Virus, *HPV* Human Papillomavirus

* *n* = 136

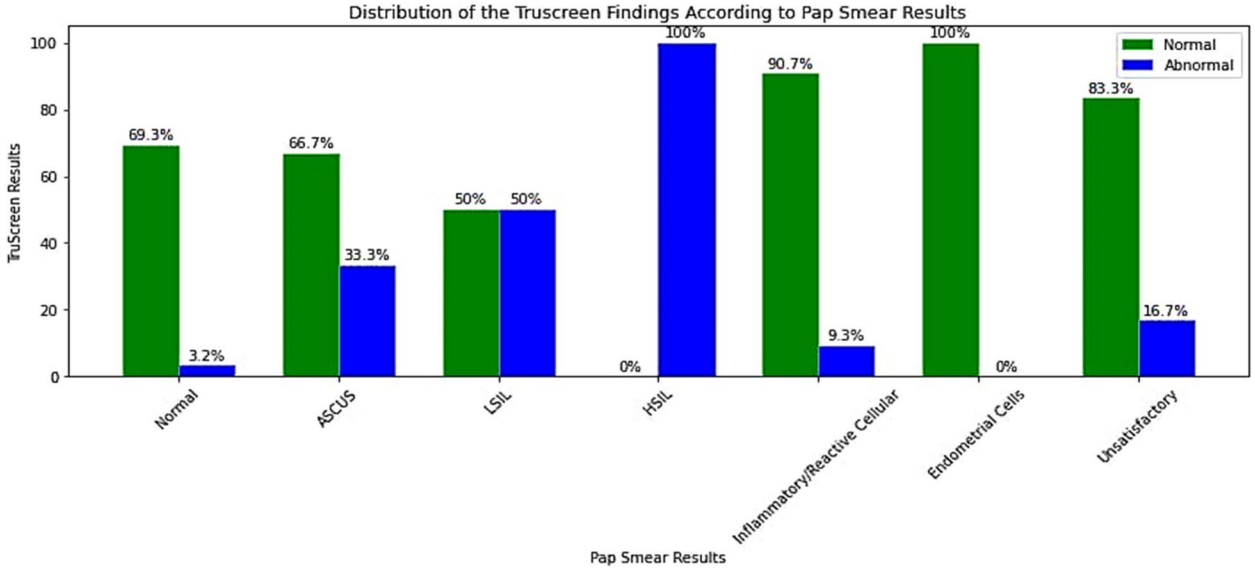

Fig. 4 Distribution of TruScreen Findingd According to Pap Smear Results. Abbreviations; ASCUS: atypical squamous cells of undetermined significance, HSIL: high-grade squamous intraepithelial lesions, LSIL: low-grade squamous intraepithelial lesions

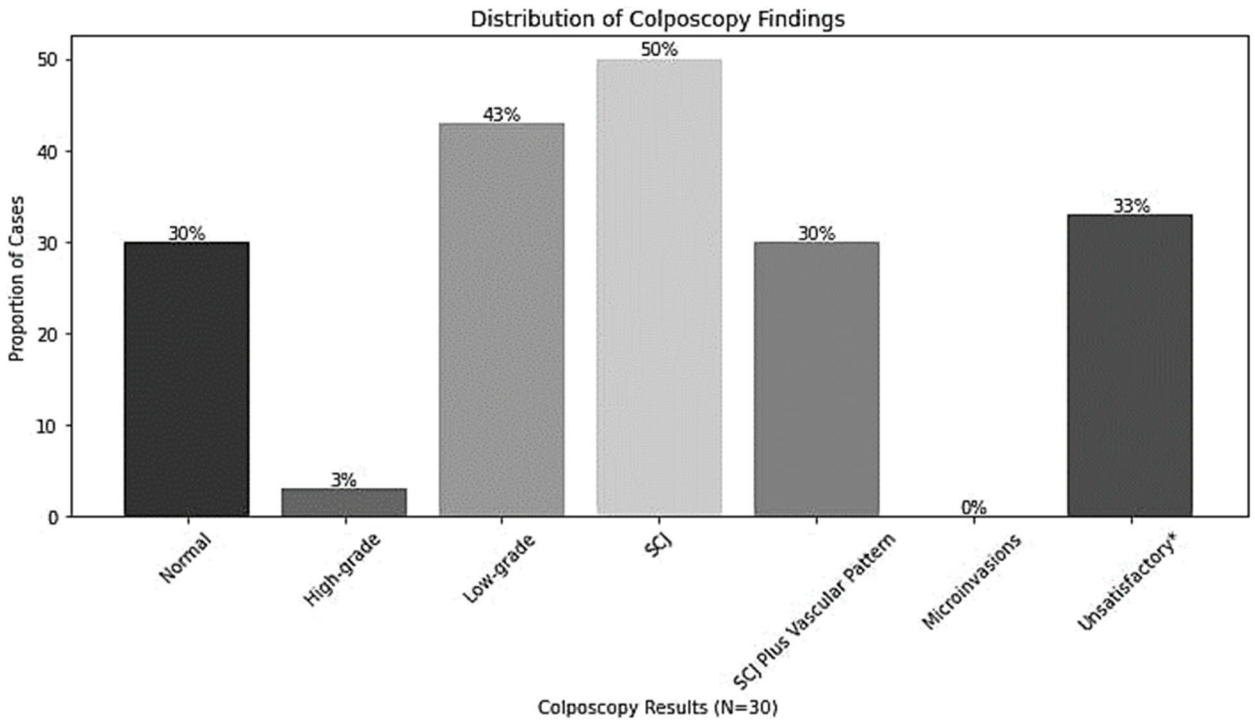

Fig. 5 Distribution of Colposcopy Findings. *Unsatisfactory colposcopy results indicate that the squamocolumnar junction cannot be visualized. Abbreviations; SCJ: squamocolumnar junction

(95% CI: 96.6%—99.2%) for the Pap smear, respectively. For CIN 2+ lesions, the sensitivity (100%; 95% CI 15.8% – 100%) and specificity (95.6%; 95% CI 93.4%—97.2%) of TS and the sensitivity (100%; 95% CI 15.8% – 100%) and specificity (98.6%; 95% CI 97.1—99.4%) of the Pap smear were both high. There was no significant difference in TS and Pap smear screening performance concerning glandular hyperplasia (Table 2).

When we combined the TS and Pap smear, the following diagnostic parameters were observed: for pathologically diagnosed cervical neoplasms, the sensitivity was 100% (95% CI: 54.1%—100%), and the specificity was 99.8% (95% CI: 98.89% – 99.9%). For women with CIN 1, the sensitivity was 100% (95% CI: 54.1%—100%), and the specificity was 99.8% (95% CI: 98.89% – 99.99%). While for CIN 2+ lesions, the sensitivity was 100% (95% CI: 54.1%—100%), and the specificity was 99.80% (95% CI: 98.89% – 99.99%). These findings reflect TS's perfect agreement in diagnosing the five pathologically confirmed cases of cervical neoplasia. However, due to the extremely limited sample size, including only five cases of cervical neoplasia, these results should be treated cautiously. Further research with a larger cohort is required to assess the diagnostic accuracy of the combined TS and Pap smear approach.

Discussion

Several developed countries have experienced significant reductions in cervical cancer incidence and cause-specific mortality in recent years, largely due to the implementation of national screening programs [26–28]. Still, the incidence and mortality of cervical cancer are considerable in the Middle East region and have increased over the period from 2000 to 2017 [29]. While such an increase can be attributed to improved access to healthcare services and lifestyle changes [29], previous reports have suggested that suboptimal implementation of screening programs and the unavailability of trained staff were also major contributors [30].

While cytology is considered the main screening tool in Middle Eastern countries, including Saudi Arabia, it has several disadvantages, including the need for cervical sampling, laboratory equipment, and trained cytopathologists. These all limit accessibility to cytology in rural and low-resource settings. Besides, the cultural acceptance of a Pap smear may be limited in some parts of the world [31–33]. Therefore, there is an unmet need to adopt a more practical but accurate tool for cervical cancer screening. TS can provide a rapid and practical assessment of cervical neoplasms by detecting the voltage response to different frequencies applied to the cervical tissue [18]. While the TS cannot determine the degree of abnormalities, a growing body of evidence has demonstrated that TS has a high screening yield in detecting cervical neoplasms [34]. A comparative study between TS and the conventional Pap test at the Whittington Hospital in London found that TS was associated with significantly less pain, pressure, and scraping compared to the spatula or brushes used to collect cells from the cervix in cytology-based screening [22]. Additionally, women strongly preferred access to an immediate result [22].

The present study showed that the real-time TS had high sensitivity (83.3%) and specificity (95%) for detecting cervical neoplasia, comparable to LBC results. The screening performance of TS was consistent across the CIN 1, CIN 2+, and glandular hyperplasia lesions (sensitivity ranging from 66.7 to 100% and specificity of nearly 96%). Besides, the TS showed a high PPV, highlighting its role in reducing the cost associated with screening by lowering the number of women who unnecessarily undergo colposcopy and biopsy. Additionally, our results showed that the positive rate of TS increased markedly with increasing severity of lesions.

Additionally, LBC findings interestingly revealed that ASC-US prevalence was 0.6%, reflecting a lower percentage than the established higher percentages. This discrepancy may be attributed to the relatively small sample size, different population characteristics, and the pilot nature of our study. Despite the lower prevalence, the ASC-US group is clinically significant, as these cases often represent a diagnostic challenge for pathologists (who use it as a safe alternative to LSIL) in our region due to potential overdiagnosis of LSIL and related social implications in the Saudi culture.

Our findings align with a previous prospective study showing that TS had a sensitivity and NPV of 86.1% and 89.5%, respectively, for detecting cervical pathologies [34]. Moreover, a more recent report showed that TS had a sensitivity and specificity of 96.3% and 46.4%, respectively, for detecting CIN 2+ in HPV-positive patients [19]. In a previous meta-analysis, TS had a sensitivity and specificity of 76% and 69%, respectively [35].

Other reports have shown lower TS sensitivity than our results. For example, Campos et al. reported a sensitivity of 43% for detecting high-grade intraepithelial lesions. However, the study showed good-to-excellent agreement between TS and colposcopy [18]. This discrepancy in the published literature can be attributed to the difference in the screened population, the standard detection method, and/or methodological differences in calculating the screening performance of TS.

Combining TS with a Pap smear may be beneficial in specific clinical settings where maximizing diagnostic accuracy is critical. For example, this approach could benefit high-risk populations, including women with persistent HPV infection, immunosuppression, or prior cervical abnormalities. Additionally, unnecessary referrals for colposcopy may be minimized by enhancing triage efficiency in low-resource settings. This combination could also help to prioritize high-risk cases for follow-up in regions with limited colposcopy access. Therefore,

Table 2 Screening Performance of TruScreen and Pap Smear

Statistic	TruScreen			Pap smear			Combined Pap + Trusscreen			*P*-value*
	No/total	*Value*	*95% CI*	*No/total*	*Value*	*95% CI*	*No/total*	*Value*	*95% CI*	
Detection of abnormal cases (*n* = 6)										
Sensitivity	5/6	83.3%	35.9% to 99.6%	4/6	66.7%	22.3% to 95.7%	6/6	100%	54.1% to 100.0%	0.910[#]
Specificity	476/501	95%	92.7% to 96.8%	492/501	98.2%	96.6% to 99.2%	500/501	99.80%	98.89% to 99.99%	
Positive Predictive Value	5/5	100%	54.1% to 100.0%	4/4	100%	54.1% to 100%	5/5	100%	54.1% to 100.0%	
Negative Predictive Value	467/467	100%	54.1% to 100.0%	492/492	100%	54.1% to 100%	500/500	100%	54.1% to 100%	
Detection of CIN I (*n* = 3)										
Sensitivity	2/3	66.7%	12.5–98%	2/3	66.7%	12.5–98%	3/3	100%	54.1% to 100%	––
Specificity	476/498	95.6%	93.4% to 97.2%	492/501	98.2%	96.6% to 99.2%	500/501	99.80%	98.89% to 99.99%	
Positive Predictive Value	2/2	100%	20.0–100%	2/2	100%	20–100%	3/3	100%	54.1% to 100.0%	
Negative Predictive Value	467/467	100%	54.1% to 100%	492/492	100%	54.07% to 100%	500/500	100%	54.1% to 100%	
CIN II + (*n* = 2)										
Sensitivity	2/2	100%	15.81% to 100%	2/2	100%	15.8% to 100%	2/2	100%	54.1% to 100%	–-
Specificity	476/499	95.3%	93.2% to 97.1%	492/499	98.6%	97.1% to 99.4%	500/501	99.80%	98.89% to 99.99%	
Positive Predictive Value	1/1	100%	15.8% to 100%	1/1	100%	15.8% to 100%	2/2	100%	54.1% to 100.0%	
Negative Predictive Value	467/467	100%	54.07% to 100%	492/492	100%	54.07% to 100%	500/500	100%	54.1% to 100%	
Glandular hyperplasia (*n* = 1)										
Sensitivity	1/1	100%	5.5 to 100%	0/1	0%	0 to 94%	1/1	100%	54.1% to 100%	0.761
Specificity	476/500	95.2%	92.9% to 96.9%	492/500	98.4%	96.8% to 99.3%	500/501	99.80%	98.89% to 99.99%	
Positive Predictive Value	1/1	100%	5.5 to 100%	0/1	0%	0 to 94%	1/1	100%	54.1% to 100.0%	
Negative Predictive Value	467/467	100%	54.1% to 100.0%	492/492	100%	54.1% to 100%	500/500	100%	54.1% to 100%	

[#] Chi-square with Fisher's exact

[*] For Truscreen versus Pap smear

implementing this co-testing can be a strategic solution in selected clinical contexts rather than routine practice.

A growing body of literature has shown that combining TS with other modalities can yield higher accuracy and reduce the need for colposcopy. Wei et al. reported that TS had higher sensitivity and specificity than the Pap smear. Still, when the two were combined, the sensitivity and specificity increased [21], which is consistent with our results. The approach that exhibited the highest sensitivity (96.3%) and specificity (83.6%) for CIN 2+ was the combination of HPV16/18 and TS (both positive) [19]. However, we acknowledge the inherent trade-off between sensitivity and specificity when co-testing is employed. Sensitivity can be increased if positive results appear with follow-up, but this will come at the expense of specificity because of more false positives. Conversely, acting only on cases where both tests are positive (+/+) may miss some true positives, reducing sensitivity.

In a recent study, a thin-layer liquid-based cytology test (TCT) combined with HPV had a considerably lower specificity (39.9%) than HPV combined with TS (50%) for CIN 2+ in women with high-risk HPV positivity, while the sensitivity for the two combinations was comparable (93.94% vs. 87.88%). Similar patterns were also observed in patients with CIN 3+ [21]. Hence, a TS and HPV combination has the excellent potential to provide effective cervical cancer screening. Studies from Poland showed similar findings [36–38]. We also acknowledge the trend toward using HPV testing as a primary screening tool, particularly with its high diagnostic capabilities. However, TruScreen can be a feasible alternative in specific scenarios, particularly in resource-limited settings where access to HPV testing is constrained by high costs and infrastructure requirements. It is also suitable in areas requiring mass screening for the same constraints. Further research is needed to analyze and verify the validity of this finding.

To our knowledge, this study represents the first observational pilot study to evaluate the feasibility and diagnostic performance of TruScreen and Pap smear in detecting cervical abnormalities in the Middle East. While the sample size of 507 participants exceeds the typical range for pilot studies, it allows for a robust initial assessment of these screening tools. As a pilot study, this research provides valuable preliminary data that can inform the design of larger, population-based studies to validate these findings and assess their generalizability. While the prospective data collection design is a strength, the relatively small sample size, depending on the pilot nature of the study, particularly among women referred for colposcopy, limits the study's power to draw definitive conclusions. Additionally, sensitivity and specificity may be inflated by only undergoing abnormal screened results. This approach, however, adhering to the clinical practice and the ethical code, prohibited the undergoing of unsuspicious cases in an invasive intervention; it may have resulted in neglecting the false negative cases. Furthermore, one limitation of our study is the lack of access to the pNOR (Probability of Normal) parameter in TruScreen, which could have provided additional insights into the device's diagnostic accuracy. Future studies should explore integrating pNOR values with Receiver Operating Characteristic (ROC) curve analysis to optimize screening performance and determine ideal cutoff thresholds. Consequently, these findings should be considered preliminary and exploratory, warranting further investigation with a larger, more representative population with better-randomized sampling in the normal group. Given the study's limitations, its results may be best interpreted as a pilot study to inform future research on the potential of TS as a cervical cancer screening tool in the region. Additionally, the multicentre approach provides a broader basis for future research and helps address potential variability in clinical workflows.

Conclusion

TS demonstrates potential as a reliable and practical screening tool for cervical neoplasms, offering the advantage of not requiring cervical samples, laboratory equipment, or highly trained personnel. While doctors conducted the examinations in this study, nurses could potentially be trained to perform TS independently within screening programs. TS enabled rapid screening with accurate results in most cases evaluated. Moreover, TS could potentially facilitate a see-and-treat approach, although further evidence is necessary to substantiate this claim.

Our findings provide preliminary support for considering TS as a potential component of cervical cancer screening strategies in countries lacking established national programs. However, additional research is imperative to validate the clinical efficacy of TS in the Middle Eastern population, particularly regarding the management of ASC-US cases that were not biopsied in this study.

Abbreviations

TS	TruScreen™
LBC	Liquid Based Cytology
CIN	Cervical Intraepithelial Neoplasia
GLOBOCAN	Global Cancer Statistics
HPV	Human papillomavirus
WHO	World Health Organization
LEEP	Loop electrosurgical excision procedure
VIA	Visual inspection with acetic acid
STARD	The Standards for Reporting Diagnostic Accuracy
IRB	Institutional review board
HIV	Human immunodeficiency virus
SD	Standard deviation
CI	Confidence Interval

PPV	Positive predictive value
NPV	Negative predictive value
ASC-US	Atypical squamous cells of undetermined significance
HSIL	High-grade squamous intraepithelial lesions
LSIL	Low-grade squamous intraepithelial lesions

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Authors' contributions
Dr. Majed Alhudhud and Dr Mazen Bishtawi conceived and designed the analysis. Dr. Maab El Hussien collected the data and performed the analysis Dr Shazia Maqsood, Dr Hiba Sarhan, DR Sadia Aslam and Dr Rifat Shaheen provided data and analysis tools and contributed to patients' recruitment. Dr Amina Butt interpreted the data and helped with the creation of the software data collection. Dr. Majed Alhudhud wrote the manuscript. Dr Mazen Bishtawi reviewed the manuscript. Dr Hisham AlKhalidi reviewed the manuscript.

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Data availability
Data and materials are available from the corresponding author (Dr Majed Alhudhud) on reasonable request.

Declarations

Ethics approval and consent to participate
The study was conducted in accordance with the Declaration of Helsinki, and the protocol was approved by the Ethics Committee of the institutional review board (IRB) (Ref No. Dr. Sulaiman Al-Habib Medical Group – RC20.08.91-Aug 2020).
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Consent for publication
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Competing interests
The authors declare no competing interests.

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