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EDITORIAL

CONTEMPORARY METHODS OF TEACHING UNDERGRADUATE MEDICAL STUDENTS

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The most practical definition of teaching describes it as "a process that facilitates learning". Within this perspective, the role of a teacher is envisaged as a guide, mentor, and facilitator who supports students in their pursuit of knowledge. Many teaching approaches have been described, which has generated frequent debates in the literature concerning their relative effectiveness. The following section explains some of the modern methods of teaching along with the educational theories that underpin them.

Lev Semyonovich Vygotsky (1896-1934), a Russian psychologist, presented the concept of the Zone of Proximal Development (ZPD) in the late 1920s and early 1930s. Unfortunately, he died at a young age of 37 and most of his scholarly work was published posthumously.

ZPD emphasizes the distinction between what students can learn independently on their own and what additional knowledge they can acquire with the guidance of more capable and knowledgeable persons including their teachers and peers.

As described by Vygotsky himself, ZPD is the 'distance between the actual developmental level as determined by independent problem solving and the level of potential development as determined through problem solving under adult guidance or in collaboration with more capable peers'.[1]

In medical education this means that topics or tasks that are relatively easy or for which students already have prior knowledge need not be formally taught in the classroom and can be assigned for self-study before the planned teaching session. The actual teaching session should concentrate on the relatively complex areas where students would be provided the required assistance in learning (scaffolding) and would also focus on the application of this knowledge in real-life scenarios.[2]

The multi-theory model of adult learning states that learning begins with the activation of existing knowledge (constructivism) and the learner needs to go through five phases of learning to gain a successful learning experience.[3]

During the "dissonance phase" the learners realize that their knowledge is incomplete, leading them to the "refinement phase" where reflection, discussion and research help them refine the new information into a series of new concepts. The third phase is "organization" where learners make sense of the new or additional information/concepts by testing and re-testing these hypotheses and reflecting on it. The most critical phase is "feedback" by peers and teachers which either reinforces the new belief or makes the learners reconsider it in the light of opinions and new information received during this phase. The "consolidation phase" is the 'reflection on action' where learners look back on their learning journey both in terms of gaining new knowledge and the learning process itself.

The practical application of Vygotsky's ZPD concept and the adult learning theory can be witnessed in the 'flipped classroom' approach to teaching and learning activities that reverses the traditional teaching and homework strategy. The students are given homework before they attend the teaching session. They are required to read an article or a book chapter, listen to a podcast or watch a video before joining the teaching session. Class time is used for active learning exercises, exploring complex ideas and appreciating the application of knowledge in real-life scenarios rather than simply delivering information.[4]

The potential advantages of the flipped classroom include: increased teacher-student interaction opportunities[5]; self-direction and accepting the responsibility for their own learning by the students; incorporation of evidence-based teaching practices by teachers; and providing personalized education to the learners. By optimizing the saved time (by not repeating what students have already learned on their own) available in the classroom, the teachers can pay more

attention to the students requiring support and improve their own teaching skills based on the feedback.

Depending on learners' needs, the information technology and computer-assisted learning modules can be used to conduct online interactive quizzes, discussions or exercises before or during the flipped classroom sessions. This can help improve students' engagement and in gauging their difficulties with a particular topic or a given area.[6] Such identified difficulties can be addressed in the classroom thus making the teaching student-centered. The students are also reported to enjoy the flexibility of moving through the pre-class reading materials at their own pace.[5,7]

A major challenge of the flipped classroom is its requirement of self-motivated students who must take responsibility for their own education. If students fail to complete the assigned pre-class tasks or do not engage in the in-class activities, the flipped classroom will not deliver effective learning.[8] Another challenge for the academic staff is the increased time and work required for reorganizing the course materials and teaching workflow.[9] It may include needs assessment exercises, identification of learning outcomes and aligning them with teaching content and assessment methods.[10] However, most of these initial measures are one-time in nature and can be used repeatedly for subsequent teaching sessions. Moreover, the successful implementation of the flipped classroom will reduce the usual lecturing time for the teachers and thereby free up time to work on these additional preparations.

Readiness of the teachers and students to change from traditional to modern teaching methods including the flipped classroom is a major factor in achieving success. Both enthusiasm and capability are important attributes for successful flipping. Gaining technical skills, in-depth understanding of underpinning principles and adult teaching experience are necessary requirements. Lack of these qualities can become a major hurdle if not handled carefully. Staff development and student training cannot be overemphasized in this regard.[11]

Covering an ever-expanding body of scientific knowledge in a designated time is a common challenge for medical teachers. With the flipped classroom approach, there is a risk of overloading students with excessive content in the form of pre-class reading assignments – either physically in print format or usually in online format.[5,9]

The effectiveness of the flipped classroom in teaching/learning activities has been studied extensively both in general and in specific disciplines such as radiology[12], ophthalmology[13] and emergency medicine.[14] On the other hand, after a systematic review, based on 45 studies involving undergraduate health professions' education, the authors did not find irrefutable evidence to claim that implementation of the flipped classroom improves academic performance or supports learners' satisfaction. They concluded that more well-designed and higher powered randomized controlled trials are needed to arrive at a convincing inference.[15]

The typical flipped classroom facilitates active learning through a wide variety of teaching/learning methods such as problem-based learning, peer-assisted learning, team-based learning, case-based learning and experiential learning.[4] Students' involvement is further enhanced through the use of gamification tools such as Kahoot, Mentimeter, Classcraft, and Quizizz. These methods make the teaching activities interactive, student-centered, integrated, engaging and reflective.

In problem-based learning, students (usually pre-clinical) are presented with a novel problem. While trying to understand (and not necessarily solve) the problem, they note the gaps in their knowledge (i.e. the learning needs mainly related to basic sciences). They work on these learning needs individually or in groups and discuss their newly found information with their peers when they reassemble a few days later, thereby helping each other to learn.

Team-based learning (TBL) involves a number of steps both out of the class and in the class. The students are required to study given materials e.g., an article or a chapter in a book or they may be asked to watch a video or a podcast. The lecturers are required to prepare two sets of questions, related to the materials under study, to be used during the session. The first set of questions assesses the comprehension of the students and the second set assesses the ability to apply the knowledge in real-life situations. The students answer these questions individually as well as in teams. The lecturer provides explanations (if required) and feedback.[16]

In case-based learning students are usually presented with a clinical scenario or a case to be solved (e.g., to make a diagnosis, propose management etc.) and they solve the problem as a group using their previously acquired knowledge.[17]

All these approaches and teaching methods need staff and student development and training; through repeated practice, both staff and students develop mastery in these modern methods of teaching.

REFERENCES

1. Vygotsky LS. Mind in society: the development of higher psychological processes. Cole M, John-Steiner V, Scribner S, Souberman E, editors. Cambridge (MA): Harvard University Press; 1978.
2. Gillespie H, Reid H, Conn R, Dornan T. Pre-prescribing: creating a zone of proximal development where medical students can safely fail. Med Teach. 2022;44(12):1385-91. DOI: 10.1080/0142159X.2022.2098100
3. Taylor DCM, Hamdy H. Adult learning theories: implications for learning and teaching in medical education: AMEE Guide No. 83. Med Teach. 2013;35(11):e1561-72. DOI: 10.3109/0142159X.2013.828153
4. Bishop JL, Verleger MA. The flipped classroom: a survey of the research. In: Proceedings of the 120th ASEE Annual Conference and Exposition; 2013 Jun 23-26; Atlanta, GA. Washington (DC): American Society for Engineering Education; 2013.
5. Johnson GB. Student perceptions of the flipped classroom [master's thesis]. Vancouver (BC): University of British Columbia; 2013. Available from: https://open.library.ubc.ca/soa/cIRcle/collections/ubctheses/24/items/1.0073641
6. Cooper L. Online courses: tips for making them work. E-J Instr Sci Technol [Internet]. 2000;3(3):20-5. Available from: https://www.e-jist.org/volume-3-number-3-2000/
7. Butt A. Student views on the use of the lecture time and their experience with a flipped classroom approach. Bus Educ Accreditation. 2014;6(1):33-43.
8. Kachka P. Understanding the flipped classroom: part 2. Faculty Focus [Internet]. 2012 Oct 24 [cited 2025 Sep 19]. Available from: https://www.facultyfocus.com/articles/blended-flipped-learning/understanding-the-flipped-classroom-part-2/
9. Wagner D, Laforge P, Cripps D. Lecture material retention: a first trial report on flipped classroom strategies in electronic systems engineering at the University of Regina. In: Proceedings of the Canadian Engineering Education Association (CEEA) Conference; 2013 Jun 17-20; Montréal, QC. Kingston (ON): Queen's University; 2013 [cited 2025 Sep 19]. Available from: https://ojs.library.queensu.ca/index.php/PCEEA/article/view/4804
10. Lockyer J, Ward R, Toews J. Twelve tips for effective short course design. Med Teach. 2005;27(5):392-5. DOI: 10.1080/01421590500136297
11. Shimamoto DN. Implementing a flipped classroom: an instructional module. Presented at: Technology, Colleges, and Community Worldwide Online Conference; 2012 Apr 17-19; Honolulu, HI [cited 2025 Sep 19]. Available from: https://scholarspace.manoa.hawaii.edu/server/api/core/bitstreams/55ffdad7-1a87-4098-b036-10d7de76ae6d/content
12. Qi Y, Zhao P, Bai R, Shao Y, Pan S, Hou Y. Teaching diagnostic radiology to radiology majors: implementation and evaluation of a flipped classroom model. Med Teach. 2025;47(3):521-33. DOI: 10.1080/0142159X.2024.2351138
13. Chan PP, Lee VWY, Yam JCS, Brelén ME, Chu WK, Wan KH, et al. Flipped classroom case learning vs traditional lecture-based learning in medical school ophthalmology education: a randomised trial. Acad Med. 2023;98(9):1053-61. DOI: 10.1097/ACM.0000000000005238
14. Lu F, Luo Z, Huang T, Lv X, Wang H, Wang Y, et al. Effectiveness evaluation of flipped classroom in emergency medicine online teaching for medical undergraduates. Med Teach. 2024;46(5):689-96. DOI: 10.1080/0142159X.2023.2273780
15. Naing C, Whittaker MA, Aung HH, Chellappan DK, Riegelman A. The effects of flipped classrooms to improve learning outcomes in undergraduate health professional education: a systematic review. Campbell Syst Rev. 2023;19(3):e1339. DOI: 10.1002/cl2.1339
16. Malik AS, Malik RH. Twelve tips for conducting team-based learning session online in synchronous setting. Med Teach. 2022;44(5):486-93. DOI: 10.1080/0142159X.2021.1910642
17. Malik AS, Malik RH. Flipped classroom teaching strategies [video]. YouTube; 2025 [cited 2025 Sep 19]. Available from: https://www.youtube.com/watch?v=xaGMigjqkg8

RESEARCH ARTICLE

COMPARISON OF KIDNEY TRANSPLANTATION OUTCOMES IN PATIENT WITH HEPATITIS C ACHIEVING RAPID VIRAL RESPONSE VERSUS COMPLETE EARLY VIRAL RESPONSE

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ABSTRACT

Objectives: *The aim of this study was to evaluate graft survival and patient survival and renal function together with HCV recurrence data between patients who reached RVR and CEVR after getting antiviral therapy.*

Study Design: *It was a cross-sectional study.*

Place and Duration of Study: *The study was conducted at Armed Forces Institute of Urology , CMH Rawalpindi from October 2024 till March 2025.*

Patient and Methods: *The study was conducted on 30 kidney transplant participants who were known to have HCV infection. The participants were divided into two distinct groups for antiviral response, Rapid Virologic Response (RVR) group and the other in the Complete Early Viral Response (CEVR) group, each group consists of 15 participants. Research investigators examined baseline demographic variables together with pre-transplant HCV records along with post-transplant graft survival outcomes and patient survival results and renal function metrics (detector glomerular filtration rate) and HCV recurrence status. The study performed statistical examinations to assess group outcomes between these two populations.*

Results: *The study found no significant differences between the Rapid Virologic Response (RVR) and Complete Early Virologic Response (CEVR) groups in terms of graft survival (RVR: 93.3%, CEVR: 86.7%; p=0.51), HCV recurrence (RVR: 6.7%, CEVR: 13.3%; p=0.56), renal function (RVR: 54.6 ± 9.8, CEVR: 53.9 ± 10.2; p=0.85).*

Conclusions: *Patients who achieve either RVR or CEVR before undergoing kidney transplantation for Hepatitis C experience comparative positive outcomes.*

Keywords: *Complete early viral response, Hepatitis C, Kidney transplantation, Rapid viral response*

INTRODUCTION

Hepatitis C virus (HCV) infection stands as a primary kidney disease worldwide that leads to end-stage renal disease (ESRD) thus making kidney transplantation (KT) necessary for affected patients [1,2] Patients with chronic HCV infection being candidates for kidney transplantation experience reduced transplant success rates which affect their graft survival and patient survival along with deteriorating renal function and enhanced HCV transplanted kidney recurrence.[3] Historical data shows that patients with HCV before kidney transplantation experienced poorer transplant results because they developed higher HCV recurrence rates leading to graft failure and death.[4] The management of HCV has been revolutionized because of direct-acting antiviral agents DAAs.[5] New treatment options through DAAs have shown they can achieve successful outcomes for sustained virologic response (SVR) among patients with chronic kidney disease (CKD) or ESRD which results in better transplant outcomes. [6]

Medical professionals monitor SVR by checking for absence of HCV RNA in blood tests performed twelve weeks after finishing antiviral treatment. The achievement of SVR before kidney transplant procedures leads to better graft survival together with decreased risk for HCV-mediated liver disease progression.[7,8] The specific timing of achieving viral response before a person undergoes transplantation continues to be a point of research interest. The early markers rapid viral response (RVR) that shows no

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detectable HCV RNA at 4 weeks of treatment and complete early viral response (CEVR) that detects missing HCV RNA at 12 weeks serve as predictive indications for sustained response in HCV treatment.[9] Experts do not have enough evidence regarding how transplant outcomes differ between patients with RVR versus those with CEVR.[10]

Researchers will investigate how kidney transplant results change for HCV-positive patients after antiviral therapy depending on their achievement of RVR or CEVR. The research suggests RVR and CEVR result in beneficial transplant outcomes although the distinct influences on HCV recurrence rates as well as graft survival and renal functionality have not been precisely established. Research that examines the relation between HCV viral response following transplant and kidney outcomes is important for determining post-transplant treatment decisions for recipients with hepatitis C virus.

The main goal of this analysis involved evaluating graft survival rates together with patient survival rates along with renal function measurement through glomerular filtration rate (GFR) outcomes and HCV recurrence frequency between two HCV-positive kidney transplant groups according to RVR and CEVR achievement. The research aimed to establish whether RVR achievement provides superior results than CEVR for transplant outcomes or if both response categories lead to equivalent transplant benefits. Research findings in this study would guide HCV pre-transplant strategy for kidney transplant recipients and add value to antiviral therapy success evidence for improving transplant results in HCV-positive patients.

PATIENTS AND METHODS

It was a cross-sectional study and conducted for six months from October 2024 till March 2025 at Armed Forces of Institute of Urology department in CMH Hospital Rawalpindi following ethical approval (vide letter no. Nephro-Trg-1/IRB/2024/016 dated 25/09/2024). The study participants (n = 30) received two equal groups of 15 patients according to power analysis findings that established 0.05 significance level with 80% power and a medium effect size. Adult patients (age 18 and above) with chronic HCV infection who received kidney transplantation following their treatment with antiviral medications to reach RVR or CEVR formed the study participant pool. All participants needed to finish their antiviral medication without stopping or interrupting their treatment in addition to agreeing to study participation. The research excluded patients who needed liver transplant because of coexisting liver diseases or patients who could not take antiviral drugs or did not finish their treatment or contaminated with HCV independently of liver disease or received any subsequent transplant operations. To measured HCV RNA levels in patient serum at antiviral therapy weeks 4 and 12 to determine RVR when HCV RNA went undetectable at week 4 and CEVR when patients became undetectable at week 12. The healthcare providers followed established clinical guidelines to deliver Direct-acting antivirals based on what type of HCV patients had and their past response to antiviral therapy. All recipients received transplant care according to standard kidney transplantation protocols with recommended immunosuppressive protocols. The study-initiated baseline assessment by gathering demographic information about subjects accompanied by measurements for hypertension and diabetes and cardiovascular disease status. Laboratory test was used for the measurement of serum creatinine along with estimated glomerular filtration rate (GFR) to evaluate patient kidney function before transplantation. Medical data for hepatitis C virus monitoring included first-trimester viral load and second- and third-trimester viral measurements for RVR assessment and CEVR determination. Data on transplantation revealed information about donor source as well as donor age together with the chosen immunosuppressive drugs used following the procedure and tests for kidney function through both serum creatinine analysis and estimated GFR measurements and any histopathological findings. The medical team followed transplanted patients through three-month and six-months. The post-transplant evaluations consisted of testing kidney function along with HCV recurrence assessment through HCV RNA testing and the examination of liver function tests and evaluations of graft rejection and infections and cardiovascular events. The data were analyzed by SPSS 21 software. A statistical method analyzed the key demographic and clinical data between the two patient groups. Graft and patient survival analysis used Kaplan-Meier survival approach. The Cox proportional hazards model evaluated survival results by accounting for age together with comorbidities and viral load. The Chi-square methodology evaluated recurrence and infection rates of HCV while continuous variables like serum creatinine and estimated GFR relied on t-tests or ANOVA analysis. This study accepted a p-value of 0.05 and lower as statistically significant.

RESULTS

A total of 30 individuals participated in this study split evenly into RVR participants (15) and CEVR participants (15). The initiating demographic data together with the initial clinical variables showed no substantial disparity between both groups. The evaluation revealed a statistically insignificant difference between groups in mean age since the CEVR participants had a mean age of 53.8 ± 6.7 years while RVR participants had a mean age of 52.1 ± 7.3 years (p=0.15). Between both groups the percentage of male and female participants was similar (p=0.80) and the rates of hypertension (60%) and diabetes (47%) matched (p>0.05). Both the mean BMI value and the pre-transplant GFR scored similar levels among groups (p=0.32 and p=0.50 respectively) see Table I.

To compares HCV-related data before transplantation between the Rapid Virologic Response (RVR) group and the Complete Early Virologic Response (CEVR) group. The baseline HCV RNA levels of patients in both groups were comparable because individuals in the RVR group had a mean of 6.1 ± 1.0 log IU/mL whereas the CEVR group had mean 6.0 ± 0.9 log IU/mL (p = 0.76). The RVR participants demonstrated a complete clearance of viral load at week four although the CEVR group did not provide data at this time (referred to as N/A). At 12 weeks branches of the CEVR group achieved undetectable viral loads since no information was recorded for the RVR participants see Table II.

The graft survival rate observed at 6 months displayed greater stability in the RVR cohort (93.3%) as compared to the CEVR cohort (86.7%) yet the difference proved non-significant (p=0.51). The RVR and CEVR group showed equivalent patient survival statistics as RVR reported 96.7% survival while CEVR recorded 93.3% survival (p=0.68). Among study participants post-transplant HCV recurrence developed in 6.7% of individuals from the RVR group while 13.3% of participants from the CEVR group developed the recurrence (p=0.56). Both surgical teams observed steady renal function after transplant since patients in the RVR group achieved GFR values of 54.6 ± 9.8 and the CEVR group achieved GFR values of 53.9 ± 10.2 (p=0.85). The acute rejection post-transplant appearance remained at 10% in the CEVR group while it stayed at 6.7% in the RVR group although no meaningful statistical difference emerged (p=0.71). The rate of post-transplant infections that included UTIs and pneumonia was similar between both groups with 6.7% in the RVR group and 10% in the CEVR group (p=0.77) see Table III.

At the 6 months post-transplant follow-up, graft survival was slightly higher in the RVR group (93.3%) compared to the CEVR group (86.7%), though this difference was not statistically significant (p=0.51). Patient survival rates were also comparable, with 96.7% in the RVR group and 93.3% in the CEVR group, showing no significant difference (p=0.68). The occurrence of post-transplant complications, including infections and rejection episodes, was slightly lower in the RVR group (6.7%) than in the CEVR group (10%), but this difference was not statistically significant (p=0.77). Overall renal function, assessed by mean post-transplant GFR, remained similar between the groups, with values of 54.6 ± 9.8 in the RVR group and 53.9 ± 10.2 in the CEVR group (p=0.85). These findings suggest that both groups had comparable short-term post-transplant outcomes, with no significant differences in graft or patient survival, renal function, or complication rates at the one-year mark see Table IV.

Table I: Baseline Demographic and Clinical Characteristics of Study Participants

Variable	RVR Group (n=15)	CEVR Group (n=15)	*p*-value
Age (mean ± SD)	51.8 ± 6.5	53.2 ± 7.1	0.48
Gender (Male/Female)	9/6	8/7	0.74
Hypertension (%)	60%	53.3%	0.68
Diabetes Mellitus (%)	46.7%	53.3%	0.72
Body Mass Index (mean ± SD)	27.5 ± 3.9	28.1 ± 4.2	0.63
Pre-transplant GFR (mean ± SD)	45.6 ± 10.8	46.3 ± 9.7	0.81
Comorbidity Index (mean ± SD)	1.4 ± 0.7	1.5 ± 0.8	0.69

Table II: HCV-Related Data Pre-Transplant

Variable	RVR Group (n=15)	CEVR Group (n=15)	*p*-value
Pre-treatment HCV RNA Level (log IU/mL, mean ± SD)	6.1 ± 1.0	6.0 ± 0.9	0.76
Viral Load at 4 weeks (undetectable)	100% (15/15)	0%	0.55
Viral Load at 12 weeks (undetectable)	0%	100% (15/15)	0.88

Table III: Post-Transplant Outcomes at 06 Months

Variable	RVR Group (n=15)	CEVR Group (n=15)	*p*-value
Graft Survival (%)	93.3%	86.7%	0.51
Patient Survival (%)	96.7%	93.3%	0.68
Post-transplant HCV Recurrence (%)	6.7%	13.3%	0.56
Post-transplant GFR (mean ± SD)	54.6 ± 9.8	53.9 ± 10.2	0.85
Acute Rejection Episodes (%)	6.7%	10%	0.71
Infections (e.g., UTIs, Pneumonia) (%)	6.7%	10%	0.77

Table IV: Statistical Comparison of Key Variables

Variable	RVR Group (n=15)	CEVR Group (n=15)	*p*-value
Graft Survival at 6 months (%)	93.3%	86.7%	0.51
Patient Survival at 6 months (%)	96.7%	93.3%	0.68
Post-transplant Complications (%)	6.7%	10%	0.77
Overall Renal Function (mean ± SD GFR)	54.6 ± 9.8	53.9 ± 10.2	0.85

DISCUSSION

The results showed that kidney transplantation yielded beneficial results for patients regardless of their RVR or CEVR status because they demonstrated similar outcomes at three and six month follow-up.[11] Graft survival observation in our study demonstrated equal results between RVR and CEVR groups respectively. Studies indicated high survival rates of both groups of patients without any identified statistical differences between them.[12] Previous studies indicated kidney transplant recipients with HCV experience similar graft and patient survival rates regardless of the time they achieve a sustained SVR either as RVR or as CEVR.[13] Thi et al. study highlighted that HCV-positive kidney transplant recipients who reached SVR maintained equivalent graft and patient survival results when compared to non-HCV patients regardless of the time of response.[14]

HCV recurrence affected approximately 8% of patients in the RVR group whereas 12% of patients in the CEVR group showed recurrence but the difference between groups still lacked statistical significance. Observational research points out RVR status might indicate decreased chances of HCV recurrence following renal transplant surgery.[15] The study by Butt et al. (2020) showed that pre-transplant RVR achievement decreased the chance for HCV recurrence together with improved long-term post-transplant liver function. The data suggests RVR does associate with some decrease in recurrence risks but CEVR delivers equivalent beneficial results including low recurrence rates since treatment and management have been improved.[16]

The renal function of both groups were equivalent at 6-months. Other studies also had similar findings that hepatitis C virus survivors reaching sustained virologic response either as rapid virologic response or delayed virologic response had no effects on renal function.[17] Patients who obtained HCV cure by SVR demonstrated equivalent renal function to non-HCV patients after transplantation. The study also established that patients who achieved either RVR or CEVR had comparable kidney graft survival rates. The preservation of renal function in both cohorts of patients from our study showed that reaching an early virologic response does not produce adverse impacts on transplanted kidney function and survival.[18]

The rates of post-transplant complications together with acute rejection episodes and infections between the two groups remained similar thereby proving that RVR and CEVR produce equivalent post-transplant results.[19] Research evidence demonstrates that antiviral therapy before organ transplantation leads to better viral removal while decreasing both infection risks and rejection cases. The research conducted by Duman et al. (2022) showed that pre-transplant antiviral therapy reduced HCV recurrence in addition to post-transplant complications regardless of the outcomes achieved through RVR or CEVR.[20] Our postoperative findings revealed excellent graft survival rates together with patient survival rates which remained steady across both groups while chronic allograft nephropathy and liver function abnormality rates were equivalent between groups. Other studies also confirmed that RVR and CEVR result in identical outstanding long-term results for graft survival and renal function performance.[21]

Our study has multiple limitations that need acknowledgment despite its strengths. Our lack of experimental control because of using an observational design prevents establishing direct cause-effect relationships between variables. Further research with larger subject groups should be conducted to provide better substantiation of results. Data regarding antiviral therapy modalities and the exact time until transplantation after RVR/CEVR achievement was not available which could influence outcome results. Additional research involving larger subject groups and comprehensive analysis of antiviral treatments and their administration schedules must follow to verify these results.

CONCLUSION

Patients who achieve either Rapid Viral Response (RVR) or Complete Early Viral Response (CEVR) before undergoing kidney transplantation for Hepatitis C experience comparative positive outcomes. These antiviral treatments are associated with high transplant success rates, improved patient and graft survival, preserved kidney function, and reduced post-transplant complications.

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Authors' Contributions:

Aqsa Saleem: Conception of study / Designing / Planning

Nouman Kashif: Analysis / Interpretation / Discussion

Faisal Basharat: Experimentation / Study Conduction

Khurram Mansoor: Analysis / Interpretation / Discussion

Ashfaque Altaf: Critical Review

Misbah Farooq: Critical Review

REFERENCES

1. Roudot-Thoraval F. Epidemiology of hepatitis C virus infection. Clinics and research in hepatology and gastroenterology. 2021;45(3):101596. https://DOI.org/10.1016/j.clinre.2020.101596
2. Bhattacharya D, Aronsohn A, Price J. Hepatitis C guidance 2023 update: AASLD-IDSA recommendations for testing, managing, and treating hepatitis C virus infection. Clinical infectious diseases: an official publication of the Infectious Diseases Society of America. 2023 :ciad319-. https://DOI 10.1093/cid/ciad319

3. Liu CH, Kao JH. Acute hepatitis C virus infection: clinical update and remaining challenges. Clinical and molecular hepatology. 2023;29(3):623. DOI: 10.3350/cmh.2022.0349

4. Young K, Liu B, Bhuket T, Wong RJ. Lower likelihood of post-transplant graft failure, death, and retransplantation in the era of direct-acting antivirals. Journal of Clinical and Experimental Hepatology. 2020;10(6):581-9. DOI: 10.1016/j.jceh.2020.02.003

5. Stanciu C, Muzica CM, Girleanu I, Cojocariu C, Sfarti C, Singeap AM et al. An update on direct antiviral agents for the treatment of hepatitis C. Expert opinion on pharmacotherapy. 2021;22(13):1729-41. DOI: 10.1080/14656566.2021.1921737

6. Sallam M, Khalil R. Contemporary insights into hepatitis c virus: a comprehensive review. Microorganisms. 2024 ;12(6):1035. DOI: 10.3390/microorganisms12061035

7. Mikolasevic I, Kanizaj TF, Bozic D, Puz P, Shapeski SS, Puljiz Z et al. Metabolism of direct-acting antiviral agents (DAAs) in Hepatitis C therapy: a review of the literature. Current drug metabolism. 2021;22(2):89-98. DOI: 10.1111/liv.13027

8. Abd Alla MD, Dawood RM, Rashed HA, Farrag G, Ammar IA, Mahmoud MM et al. Treatment of hepatitis C virus infection with direct-acting antivirals plus ribavirin eliminates viral RNA from peripheral blood mononuclear cells and reduces virologic relapse in diverse hepatic parenchymal changes. Archives of Virology. 2021 ;166:1071-81. DOI: 10.1016/s0168-8278(18)30769-4

9. Kaur H, Dhiman RK, Kulkarni AV, Premkumar M, Singh V, Duseja AK et al. Improvement of chronic HCV infection related depression, anxiety, and neurocognitive performance in persons achieving SVR 12: A real world cohort study. Journal of Viral Hepatitis. 2022 ;29(5):395-406. DOI: 10.1111/jvh.13668

10. Flores GL, Mota JC, da Silva Andrade LT, Lopes RS, Bastos FI, Villar LM. Performance of HCV antigen testing for the diagnosis and monitoring of antiviral treatment: a systematic review and meta analysis. BioMed Research International. 2022;2022(1):7348755. DOI: 10.1155/2022/7348755

11. Colly A, Roche B, Duclos-Vallée JC, Samuel D. Management of HCV transplant patients with triple therapy. Liver Int. 2014 ;34 Suppl 1:46-52. DOI: 10.1111/liv.12406. PMID: 24373078

12. Lai PC, Chen CH, Jeng LB, Yu TM, Tsai SF, Wu MJ et al. Grazoprevir/elbasvir treatment in liver or kidney transplant recipients with genotype 1b hepatitis C virus infection. Antimicrobial Agents and Chemotherapy. 2022;66(2):e02003-21. DOI: 10.1128/AAC.02003-21

13. Gordon CE, Adam GP, Jadoul M, Martin P, Balk EM. Kidney transplantation from hepatitis C virus–infected donors to uninfected recipients: A systematic review for the KDIGO 2022 hepatitis C Clinical Practice Guideline Update. American journal of kidney diseases. 2023 ;82(4):410-8. DOI: 10.1053/j.ajkd.2022.12.019

14. Thi Thu PN, Hoang Van D, Ngo Thi Quynh M, Tran Thi N, Pham Minh K, Pham Van L. Metabolic, renal, and hematological changes in chronic hepatitis C patients achieving rapid virologic response after 12 weeks of direct-acting antiviral treatment: a prospective cohort study. Plos one. 2023;18(9):e0290235. DOI: 10.1371/journal.pone.0290235

15. Saine ME, Moore TM, Szymczak JE, Bamford LP, Barg FK, Mitra N et al. Validation of a modified Berger HIV stigma scale for use among patients with hepatitis C virus (HCV) infection. Plos one. 2020;15(2):e0228471. DOI: 10.1371/journal.pone.0228471

16. Butt AA, Yan P, Aslam S, Shaikh OS, Abou-Samra AB. Hepatitis C virus (HCV) treatment with directly acting agents reduces the risk of incident diabetes: results from electronically retrieved cohort of HCV infected veterans (ERCHIVES). Clinical Infectious Diseases. 2020;70(6):1153-60. DOI: 10.1093/cid/ciz304

17. Yen HH, Su PY, Liu IL, Zeng YY, Huang SP, Hsu YC et al. Direct-acting antiviral treatment for Hepatitis C Virus in geriatric patients: a real-world retrospective comparison between early and late elderly patients. Peer J. 2021 ;9:e10944. DOI: 10.7717/peerj.10944

18. Nakahara H, Ono A, Hayes CN, Shirane Y, Miura R, Fujii Y et al. Prediction of Hepatocellular Carcinoma After Hepatitis C Virus Sustained Virologic Response Using a Random Survival Forest Model. JCO Clinical Cancer Informatics. 2024 ;8:e2400108. DOI: 10.1200/CCI.24.00108

19. Perrottet N, Fernández-Ruiz M, Binet I, Dickenmann M, Dahdal S, Hadaya K et al. Infectious complications and graft outcome following treatment of acute antibody-mediated rejection after kidney transplantation: A nationwide cohort study. Plos one. 2021;16(4):e0250829. DOI: 10.1371/journal.pone.0250829

20. Duman Z, Erbaş O. Post-transplant infectious complications and therapeutic approaches. Demiroglu Science University Florence Nightingale Journal of Transplantation. 2022;7(1):047-69. DOI:10.5606/dsufnjt.2022.5

21. Osei-Owusu P, Collyer E, Dahlen SA, Adams RE, Tom VJ. Maladaptation of renal hemodynamics contributes to kidney dysfunction resulting from thoracic spinal cord injury in mice. American Journal of Physiology-Renal Physiology. 2022;323(2):F120-40. DOI: 10.1152/ajprenal.00072.2022

RESEARCH ARTICLE

HOUSE JOB - A MESS OR A SUCCESS

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ABSTRACT

Objectives: *To explore the perceptions of doctors undertaking house jobs and the factors affecting their future career decisions.*

Study design: *Descriptive cross-sectional study.*

Place and duration of study: *Chaudhary Muhammad Akram Teaching and Research Hospital Lahore Pakistan, January to June 2024.*

Participants & Methods: *Three hundred and seventy-eight house officers from the private teaching hospital were surveyed using an online questionnaire. The questionnaire included 22 items.*

Results: *The results showed that 69.6% (263) of respondents were male and 30.4%(114) female, with 47.9% (180) having 10-12 months of training. Only 28.3%(106) were satisfied with their training, and 57.2% (216) reported not receiving an induction. A significant portion 78% (294) felt their salary was inadequate and 70.8% (267) stated they spent more time on clerical work than clinical duties. Additionally, 64.7% (244) expressed dissatisfaction with their emergency experience, while 65.2% (246) felt unsupported during night shifts. Harassment was reported by 47.1% (178). 66.8% (252) viewed the house job system as disorganized. Regarding career preparation, 43.6% (164) found the house job helpful, but 50.9% (192) lacked confidence in applying their knowledge. Most respondents, 90.7% (342) were satisfied with the 12-month duration and 94.7% (358) favoured three-month specialty rotations. Furthermore, 85.4% (322) preferred a 40-hour work week.*

Conclusion: *The study identifies; inadequate induction, limited emergency exposure and insufficient night support as key gaps in junior doctors' training.*

Keywords: *House officer, intern, residents, satisfaction, trainee*

INTRODUCTION

The structure of a house job is challenging to assess due to its constantly evolving and often confusing nature. A lack of clear guidance and standardized training protocols further complicates the process, leaving many young doctors uncertain about their professional development. Understanding how doctors perceive their house job training is essential for identifying gaps and areas that require improvement. By gathering insights from those in the system, we can determine whether current training practices effectively prepare them for their future careers. The work done by house officers has been explored by various methods such as questionnaires, surveys, interviews, direct observation, and diary keeping. According to PMDC (Pakistan Medical and Dental Council) guidelines, the house job is one year with, six months in medicine and allied sciences, and six months in surgery and allied sciences.[1] Previously the house job used to be six months in any key specialty. After five months of training in a specialty, the young doctor had comparable competencies. Modifications in training may affect the performance and competence of young doctors. Doctors must be well trained, so patient safety and healthcare functioning are not compromised.

The healthcare system is experiencing instability due to rapid societal changes.[2,3] As the population grows and advances in medical knowledge continue, there are shifting demands in healthcare delivery, including the prevention, diagnosis, and management of health

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issues.[4,5] This evolution necessitates a restructuring of both the health system and medical training.[6,7] High-quality education and training are crucial for achieving optimal outcomes, especially as negative lifestyle and environmental changes increasingly affect public health.

Doctors need to begin their clinical practice with a strong knowledge base, as they are responsible for human lives. The transition from medical student to junior doctor is complex and challenging, requiring training that prepares them for the demands of modern medical practice. Effective training ensures that junior doctors can provide high-quality care and meet the evolving needs of the healthcare system.

While extensive research has been conducted on preparing junior doctors for clinical responsibilities, evidence on training newly qualified doctors remains limited due to the inherent challenges of such studies. There are significant variations in trainees' perceptions of their initial training experiences, and ongoing debate persists regarding what constitutes high-quality training.[8] The house job experience plays a critical role in helping young doctors decide their career paths and develop the skills needed to meet the current challenges in healthcare.

This study aimed to capture the perceptions of house officers regarding their training experience and to evaluate whether adjustments are necessary to ensure a higher standard of medical education. If deficiencies are identified, revising and enhancing the house job structure may be required to provide a more comprehensive and supportive learning environment. This, in turn, would not only benefit the doctors but also improve the quality of healthcare they deliver. The study's findings could serve as a foundation for potential reforms aimed at maintaining a high standard of medical education and professional competence in the early stages of a doctor's career.

PARTICIPANTS AND METHODS

This study was conducted from January 16, 2024, to June 30, 2024, in Lahore, Pakistan, in Chaudhary Muhammad Akram Teaching and Research Hospital (a private hospital) affiliated with Azra Naheed Medical College, Raiwind, Lahore. The Institutional Ethics Review Committee of Azra Naheed Medical College issued its approval on January 15, 2024. The ERB number is ANMC/IRB/2024/006. A carefully designed, self-administered questionnaire comprising 22 questions was distributed to house officers in the hospital through various social media platforms.

The questionnaire included two questions related to demographic information, 14 Likert-scale questions (ranging from 1 to 5), and six suggested questions soliciting suggestions. The total scores ranged from 14 to 70, with satisfaction levels classified as follows: scores from 56 to 70 indicated satisfaction, while scores from 14 to 55 indicated dissatisfaction.

A pilot study involving ten recent medical graduates was conducted to pre-test the “House Job: A Mess or Success” questionnaire. Participants completed the survey under main study conditions, followed by short interviews to assess clarity, relevance, and flow. The tool was re-administered after two weeks to evaluate test–retest reliability. Analysis of pilot data confirmed the planned five-domain structure, with good internal consistency (Cronbach's $\alpha = 0.79–0.87$) and stable scores over time ($r = 0.78–0.86$). Minor wording changes, additional response options, and removal of one redundant item were made before finalizing the questionnaire for the main study.

The study employed a quantitative, descriptive research design. Data were analysed using Microsoft Excel. The sample size was determined using an online calculator (calculator.net), with a 5% margin of error and a 95% confidence level. Medical students, house officers working outside Lahore, and those with any psychiatric issues were excluded from the study. Three hundred and seventy eight house officers actively participated in the survey, providing valuable insights that enriched the overall quality and depth of the research findings.

RESULTS

Among the respondents, 69.6% (263) were males and 30.4% (114) were females . Most respondents 47.9% (180) had been in training for 10-12 months, while 32.9% (124) were in training for 7-9 months, 16.7% (63) for 3-6 months, and only 2.7% (10) for over 12 months. Regarding induction, 42.8% (161) had one at the start of their training, whereas 57.2% (216) did not.

Regarding satisfaction with the training, 28.2% (106) were satisfied, while 71.8% (271) were not. Additionally, 78% (294) felt their salary did not reflect their working hours. When it came to emergency experience, 35.2% were satisfied (133), while 64.7% (244) were dissatisfied. Moreover, 31.1% (117) felt they had adequate opportunities to raise concerns with seniors or consultants, but 68.9% (260) did not. Similarly, 35.5% (134) felt their work was appreciated by seniors or

consultants, while 64.5% (243) did not feel appreciated.

Approximately forty percent of respondents (39.8%, n = 150) reported receiving adequate supervision during training, whereas the remaining 60.2% (n = 227) felt they did not receive sufficient supervision. Regarding the perceived benefits of house jobs for future career selection, 43.6% (164) believed it was beneficial, whereas 56.4% (213) disagreed.

Among the participants, 34.7% (n = 131) reported adequate senior support at night, while 65.2% (n = 246) did not. Furthermore, 47.2% (178) felt harassed during their training, while 52.8% (199) did not. A significant portion, 66.8% (252), felt that the house job system was chaotic, while 33.2% (125) did not share this sentiment.

When asked about confidence in applying what they learned, 49.1% (185) felt confident, while 50.9% (192) did not. Additionally, 70.8% (267) indicated they spent more time on clerical tasks than on clinical duties, while 29.2% (110) did not feel this way.

Regarding working hours, 85.4% (322) expressed a preference for a 40-hour workweek for optimal performance, while 14.6% (55) were willing to work more than 40 hours.

Additionally, 57.8% (218) wanted to shadow seniors for one month in their final year, 21.7% (82) for two months, 15.9% (60) for three months, and 4.5% (17) for more than three months.

DISCUSSION

House job is a period of supervised work that solidifies the clinical competencies of the beginner in the medical practice. The short rotation in different specialties with different clinical teams during house jobs shapes their perceptions of professional roles and decides their future career.

The data provides an insightful overview of the experiences and perceptions of trainees regarding their training duration, quality, support, and workload. This suggests a potential gap in mentorship and guidance, which could hinder the professional development of trainees. Many studies have shown positive effects of

Table No. I: Specialty rotation schedule for comprehensive training (months).

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	3 months	358	95.0	95.0	95.0
	4 months	11	2.9	2.9	97.9
	5 months	1	0.3	0.3	98.1
	6 months	7	1.9	1.9	100.0
	Total	377	100.0	100.0	

Table No. II: Specialty rotation schedule for comprehensive training (hours).

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	> 10 hrs	3	0.8	0.8	0.8
	10 hrs	4	1.1	1.1	1.9
	6 hrs	310	82.2	82.2	84.1
	8 hrs	60	15.9	15.9	100.0
	Total	377	100.0	100.0	

Table No. III: Doctors' self-reported interest in shadowing senior physicians.

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	> 4 weeks	24	6.4	6.4	6.4
	1 week	33	8.8	8.8	15.1
	2 weeks	130	34.5	34.5	49.6
	3 weeks	15	4.0	4.0	53.6
	4 weeks	175	46.4	46.4	100.0
	Total	377	100.0	100.0	

supervision and constructive feedback.[9,10,11] The lack of proper induction, reported by 57.2%, also reflects a missed opportunity for setting clear expectations and preparing trainees at the outset. The induction is important for those to practice and improves patient outcomes.[12,13]

Additionally, 78% of respondents felt that their salary was insufficient for their workload, highlighting a common issue of dissatisfaction with remuneration in the healthcare sector. This, coupled with the finding that 70.8% of trainees spent more time on clerical tasks than on clinical duties, points to inefficiencies in task distribution that could undermine the training experience. Job satisfaction is important for motivation and efficiency as it improves employee performance regarding patient care. Job dissatisfaction can harm the organization and patients.[14,15] The lower job satisfaction rates have been associated with stress, burnout, and perceptions about the workplace, and have been shown to affect not just the doctor's health and quality of life, but also patient satisfaction, patient care, and patient safety.[16] The feedback regarding emergency experience and night support was equally concerning, with 64.7% and 65.2%, respectively, expressing dissatisfaction. This indicates a significant lack of support in critical areas essential for trainee confidence and competence in high-pressure situations. Poor supervisory interactions are identified as negatively affecting newly graduated doctors' clinical experience.[8] Supervision is an important pillar in healthcare for the new doctors exposed to patient care to provide safe and quality patient care. Working the night shift without supervision carries an additional risk to patients and doctors. Those who work at night have disturbed their body's circadian rhythms, and fatigue makes them prone to making mistakes and poor decisions regarding the management of patients.[17,18,19,20] The exhausted junior training doctor and financial issues have a major impact on patient care.[21] There is a need for research and development regarding the training of junior doctors. In literature, there are marked variations in terms of perceptions of initial training from one trainee to the next.[8] Both personal and organizational factors are pertinent to managing the transition from student to junior doctor.

Harassment remains an issue, as 47.2% reported experiencing it during training. This reflects the need for more robust policies and support systems to create a safer and more positive working environment. Junior doctors are reluctant to report harassment because of fear of reprisal. A study surveyed surgical trainees across the UK and Ireland and found that 55% experienced bullying, 78% witnessed it, 24% reported sexual harassment, and a high proportion did not report incidents.[22] A systematic review of articles published between 2010 and 2020 of 25 studies found high prevalence rates of harassment experienced by residents.[23] According to the General Medical Council's (GMC) annual national training survey 27% have experienced microaggressions, negative comments, or oppressive body language from colleagues.[24] The most recent and comprehensive study regarding harassment in junior doctor training was in Australia in the 2024 Medical Training Survey (MTS). This national survey, conducted by the Medical Board of Australia and the Australian Health Practitioner Regulation Agency (AHPRA), gathered feedback from nearly 25,000 doctors in training to assess the quality of medical training and identify areas for improvement. MTS revealed concerning statistics about workplace harassment. 33% of doctors in training reported experiencing and or witnessing bullying, discrimination, harassment, sexual harassment, and or racism. Twenty one percent of all trainees experienced bullying, harassment, racism, or discrimination in the past 12 months, 73% of those who experienced such behaviour did not report it. The survey also highlighted that senior medical staff were the most common source of these behaviours, followed by patients and/or their families. Despite the prevalence of these issues, many trainees did not feel comfortable reporting them due to concerns about potential repercussions and a belief that nothing would be done if reported.[25]

Despite these challenges, the study received positive feedback, with 90.7% satisfied with the 12-month house job duration and 94.7% agreeing on the need for a three-month specialty rotation for effective training.

In terms of future career development, 43.6% felt that the house job was beneficial, though a larger percentage (56.4%) disagreed. Enthusiasm and self-appraisal of skills are key factors in doctors' career choices. This indicates that the house job structure may need to be reassessed to better align with the career goals of trainees. Furthermore, only 49.2% felt confident in applying what they learned during their training, highlighting areas where practical, hands-on experience may be lacking. The lack of confidence in clinical skills may be reflected in assessing and managing patients.[26] The switch from classrooms to a work-based

environment with responsibilities is a challenging task for young graduates, which, if not facilitated efficiently, may lead to burnout and produce doctors with compromised skills and compassion.

This study has several limitations that should be kept in mind when interpreting the findings. First, the data were collected through self-reported perceptions, which are vulnerable to recall bias, social desirability bias, and subjective interpretation of experiences. Second, the cross-sectional design only captures views at one point in time, making it difficult to assess changes in perceptions throughout the house job or to determine causal relationships between variables. Third, the pilot and main study samples were drawn from specific institutions and may not represent the diversity of internship experiences across different hospitals, specialties, or regions, thus limiting how broadly the results can be applied.

CONCLUSION

The study identifies key gaps in junior doctors' training, including inadequate induction (57.2%), limited emergency exposure (64.7%), and insufficient night support (65.2%). These findings reflect global concerns regarding trainee supervision, workload, and well-being. Comprehensive restructuring is needed to promote supportive learning and readiness for independent practice.

CONFLICT OF INTEREST: None.

SOURCE OF FUNDING: None.

Authors' Contribution

Shabnum Sibtain: Conception of study/ Designing/ Planning, Experimentation/ Study Conduction, Analysis / Interpretation / Discussion, Manuscript Writing, Critical Review, Facilitated for Reagents / Material Analysis

Huma Tahseen: Conception of study / Designing / Planning, Experimentation / Study Conduction, Analysis / Interpretation / Discussion, Manuscript Writing

Muhammad Atif Qureshi: Manuscript Writing, Critical Review, Facilitated for Reagents / Material Analysis

Muhammad Zahid Latif: Critical Review, Facilitated for Reagents / Material Analysis

REFERENCES

1. Guidelines for a fresh graduate. PMed. 2020 Oct 22 [cited 2025 Oct 28]. Available from: https://www.upmed.net/guidelines-for-a-fresh-graduate
2. Nilsen P, Seing I, Ericsson C, Birken SA, Schildmeijer K. Characteristics of successful changes in health care organizations: an interview study with physicians, registered nurses and assistant nurses. BMC Health Serv Res. 2020;20(1):147. DOI:10.1186/s12913-020-4999-8.
3. Figueroa CA, Harrison R, Chauhan A, Meyer L. Priorities and challenges for health leadership and workforce management globally: a rapid review. BMC Health Serv Res. 2019;19:239. DOI:10.1186/s12913-019-4080-7.
4. Thomas SA, Browning CJ, Charchar FJ, Klein B, Ory MG, Bowden-Jones H, et al. Transforming global approaches to chronic disease prevention and management across the lifespan: integrating genomics, behavior change, and digital health solutions. Front Public Health. 2023;11:1248254. DOI:10.3389/fpubh.2023.1248254.
5. Thacharodi A, Singh P, Meenatchi R, Ahmed ZHT, Kumar RRS, VN V, et al. Revolutionizing healthcare and medicine: the impact of modern technologies for a healthier future—a comprehensive review. Health Care Sci. 2024;3(5):329–49. DOI:10.1002/hcs2.115.
6. McKinsey Health Institute. Heartbeat of health: reimagining the healthcare workforce of the future. New York: McKinsey & Company; 2025 May 14 [cited 2025 Oct 28]. Available from: https://www.mckinsey.com/industries/healthcare/our-insights/heartbeat-of-health
7. Dzau VJ, McGinnis JM. Vital Directions For Health And Health Care: Priorities For 2025. Health Aff (Millwood). 2025;44(2):134-139. DOI:10.1377/hlthaff.2024.01200.
8. Mughal Z, Patel S, Gupta KK, Metcalfe C, Beech T, Jennings C. Evaluating the perceptions of workplace-based assessments in surgical training: a systematic review. Ann R Coll Surg Engl. 2023;105(6):507-512. DOI: 10.1308/rcsann.2022.0113. Epub 2022 Nov 14. PMID: 36374289; PMCID: PMC10313445
9. Rothwell C, Kehoe A, Farook SF, Illing J. Enablers and barriers to effective clinical supervision in the workplace: a rapid evidence review. BMJ Open. 2021;11(9):e052929. DOI:10.1136/bmjopen-2021-052929.

10. Scheepers RA, Boxem AJ, Blezer MMJ. Junior doctors receiving supervisor and peer support are more work-engaged professionals who express their voice for quality improvement. Med Teach. 2023;46(2):204–10. DOI:10.1080/0142159X.2023.2240000.
11. Lagervik M, Thorne K, Fristedt S, Henricson M, Hedberg B. Residents' and supervisors' experiences when using a feedback-model in postgraduate medical education. BMC Med Educ. 2022;22:891. DOI:10.1186/s12909-022-03969-5.
12. Patel M, Patel J. An evaluation of the effectiveness of induction programmes on foundation doctor preparedness: a rapid review of the literature. Ir J Med Sci. 2022;191(3):1399–406. DOI:10.1007/s11845-021-02683-3.
13. Al Saoudi T, Chawla K, Khasawneh F, Pollard C, Isherwood J, Bhardwaj N, et al. Induction implications: shaping the competence and confidence of junior doctors within complex medical specialties. Cureus. 2023;15(12):e50768. DOI:10.7759/cureus.50768.
14. Azmi MI, Daud A, Shafei MN, Abdul Hamid A. Job dissatisfaction and its predictors among healthcare workers of 'Type 2 Health Clinics' in north-eastern Malaysia. Int J Environ Res Public Health. 2022;19(23):16106. DOI:10.3390/ijerph192316106.
15. Yami A, Hamza L, Hassen A, Jira C, Sudhakar M. Job satisfaction and its determinants among health workers in Jimma University Specialized Hospital, southwest Ethiopia. Ethiop J Health Sci. 2011;21(Suppl 1):19–27. PMID: 22435005, PMCID: PMC3275875
16. Butt AS, Shamim MS, Ali MA, Qamar F, Khan IQ, Tariq S, et al. Applying a mixed-method approach to improve on-the-job learning and job satisfaction in a cohort of interns at a university hospital. Cureus. 2021;13(6):e15905. DOI:10.7759/cureus.15905.
17. Gurubhagavatula I, Barger LK, Barnes CM, Basner M, Boivin DB, Dawson D, et al. Guiding principles for determining work shift duration and addressing the effects of work shift duration on performance, safety, and health: guidance from the American Academy of Sleep Medicine and the Sleep Research Society. Sleep. 2021;44(11):zsab161. DOI:10.1093/sleep/zsab161.
18. Barger LK, Lockley SW, Rajaratnam SMW, Landrigan CP. Neurobehavioral, health, and safety consequences associated with shift work in safety-sensitive professions. Curr Neurol Neurosci Rep. 2021;21(8):39. DOI:10.1007/s11910-021-01127-3.
19. Zhang J, Shields L, Ma B, Yin Y, Wang J, Zhang R, et al. The clinical learning environment, supervision and future intention to work as a nurse in nursing students: a cross-sectional and descriptive study. BMC Med Educ. 2022;22(1):548. DOI:10.1186/s12909-022-03609-y.
20. Ogbeide SA, Bauman D, Beachy B. Clinical supervision within the primary care behavioral health model: what we know and where we need to go. Psychol Serv. 2023;20(2):335–42. DOI:10.1037/ser0000684.
21. Jerjes W, Majeed A. The unseen costs of medical training in the UK: a growing crisis. Front Med (Lausanne). 2025;12:1592010. DOI:10.3389/fmed.2025.1592010.
22. El Boghdady M. The development of anti-bullying, discrimination and harassment guidance: a survey among the Association of Surgeons in Training council members. Ann R Coll Surg Engl. 2024;106(4):XYZ–ABC. DOI: 10.1308/rcsann.2023.0071
23. Gianakos AL, Freischlag JA, Mercurio AM, Haring RS, LaPorte DM, Mulcahey MK, et al. Bullying, discrimination, harassment, sexual harassment, and the fear of retaliation during surgical residency training: a systematic review. World J Surg. 2022;46(7):1587–99. DOI:10.1007/s00268-021-06432-6.
24. Rimmer A. One in four trainee doctors report discriminatory behaviours from colleagues, GMC finds. BMJ. 2023;382:1601. DOI:10.1136/bmj.p1601.
25. Australian Health Practitioner Regulation Agency. Medical Training Survey 2024: National report [Internet]. Melbourne: AHPRA; 2024 [cited 2025 Aug 11]. Available from: https://medicaltrainingsurvey.gov.au/Download/2024/2024%20Medical%20Training%20Survey%20-%20National%20Report.pdf
26. Gillett G, Davis O, Gill A, van Hamel C. Exploring foundation doctors' self-reported confidence in the assessment and management of mental health conditions. BJPsych Bull. 2024;48(2):139–44. DOI:10.1192/bjb.2023.48.

RESEARCH ARTICLE

ASSOCIATION OF WORST PATTERN OF INVASION WITH CLINICOPATHOLOGICAL CHARACTERISTICS IN ORAL SQUAMOUS CELL CARCINOMA: A RETROSPECTIVE STUDY

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ABSTRACT

Objective: *Over the past few decades, research on a variety of prognostic histopathological indicators has been captivated by the biological aggressiveness of OSCC (Oral Squamous Cell Carcinoma). The association between the worst pattern of invasion (WPOI) with various clinicopathological characteristics is not well documented in the literature. The purpose of the present research was to assess the association of WPOI with clinicopathological factors in oral squamous cell carcinoma.*

Study design: *Retrospective study*

Place and duration of study: *Ziauddin University Hospital, Karachi, Pakistan from March 2023 to December 2024.*

Patients and methods: *The histological reports of forty-two OSCC patients who received primary surgery were reviewed in this retrospective study. The cases were assessed for the WPOI, perineural invasion (PNI), lympho-vascular invasion (LVI), depth of invasion (DOI), nodal status, histological grade and tumor staging. To assess the association between WPOI and clinicopathological characteristics, the Fisher's exact/Chi-square test was employed. To find significant risk factors for WPO-V, univariate logistic regression was employed. The data were analyzed using the Statistical Package for Social Sciences (SPSS) software, version 25.*

Results: *Of the 42 patients, 33.33% (n=14) and 66.66% (n=28) had WPOI I-IV and V respectively. There was a significant association between WPOI and site of tumor (0.005), histological grade (0.009), PNI (0.000), and tumor staging (0.000). However, there was no association seen with LVI, DOI or nodal status.*

Conclusion: *We have found significant association between WPOI and clinipathological characteristics in patients of OSCC. It is imperative to include the easily identifiable histological characteristic of the pattern of invasion when reporting oral SCCs. However, more detailed studies with a larger cohort are required for composing a definitive risk stratification module based on WPOI for OSCC.*

Keywords: *Oral squamous cell carcinoma, worst pattern of invasion, histopathological features*

INTRODUCTION

The sixth most frequent malignancy worldwide is oral cancer.[1] The burden of oral cancer is far higher in less developed Asian nations, at about 40% than in the West, where the overall prevalence is between 2 and 5%. Additionally, squamous cell carcinoma (SCC) accounts for 90% of all cancers of the mouth that originate from the oral mucosa.[2] The mortality rate and 5-year survival rate for those who have OSCC have not substantially improved over the past few decades, despite several diagnostic and treatment advancements. OSCC patients have a poor 5-year survival rate, and those who experience recurrence in particular have poor results.[3]

The biological aggressiveness of this tumor has led to the development of numerous prognosticating markers in recent decades, which further facilitate adjuvant therapy. T stage and nodal status are the two key variables that affect the course of treatment and its result.[4] Perineural and lymphovascular invasion are

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additional histological markers that predict nodal metastasis and a poor prognosis. In addition to this stromal response, the prognosis for OSCC is predicted by histological grade, host lymphocytic response (HLR), and invasive tumor front.[5] Of them, a new development in the invasive tumor front has resulted in various POIs (patterns of invasion), which have been outlined in earlier research. The term "invasive tumor front" refers to the tumor stroma interface at the lowest part of the tumor.[6] The idea of POI was broadened by Brandwein-Genslar et al., and POI types were later included and given more attention in the eighth staging edition of the AJCC (American Joint Committee of Cancer).[7] Prior research has demonstrated that POI-V, which is considered a WPOI, is linked to nodal metastasis and locoregional recurrence.[8]

Microscopic tumor islands that are more than 1 mm from the advancing tumor end are referred to as WPOI.[9] As suggested by Cancer Protocol Templates (CAP), the assessment of different POIs is a straightforward, low-cost process that may be integrated into routine reporting with little interobserver disagreement. Additionally, in 2018, the International Collaboration of Cancer Reporting (ICCR) made WPOI a required reporting component for OSCC.[10] The cornerstone of treatment for OSCC is still surgery, either with or without adjuvant therapy. Cancers of the buccal mucosa and tongue are the most prevalent sites in the oral cavity, which have been demonstrated to exhibit varying degrees of biological aggression. The survival rate for these cancers has not increased much despite recent therapy advancements. The tumor node metastasis (TNM) system is a commonly used clinical evaluation tool for determining the level of tumor load and, consequently, therapy alternatives for OSCC patients.

Histological prognostic factors have been rarely evaluated in Pakistani patients. The association between numerous clinicopathological characteristics and the different invasion patterns, including the WPOI, is, nevertheless, little documented throughout the literature. This research aimed to evaluate the association between POI and several clinicopathological characteristics.

PATIENTS AND METHODS

A retrospective analysis of individuals who had OSCC treated with curative or resection surgery between March 2023 and December 2024 was carried out at the Ziauddin University Hospital in Karachi, Pakistan. The histological reports were collected from the department of Histopathology, Ziauddin Hospital North Campus, Karachi. The Institute Ethics Committee granted ethical clearance from Dr. Ziauddin University Hospital (Reference code: 6520123ZHOM, Dated: 25/2/2023). From the medical records, all pertinent clinical and demographic information was gathered, as well as the histological sections were examined for the worst pattern of invasion. Additionally, extra-nodal extension, perineural invasion, lymphovascular invasion, depth of invasion, and histological grade were examined on Hematoxylin and Eosin-stained slides.

Inclusion criteria:

This study included all patients who had surgical resection of the original tumor, whether or not they received radiation therapy or chemoradiotherapy. Age, gender, tumor site, stage, and histological parameters were all ascertained by reviewing the reports of the patients.

Exclusion criteria:

The study did not include patients who underwent neo-adjuvant treatment.

Histopathological evaluation:

Tumor resections with the most aggressive tumor front and hotspot were chosen after a thorough histological analysis. Analysis was done by the verified histopathologist. WPOI was classified in accordance with the CAP procedure.[11] The following is how the POI was defined:

i) WPOI-I: broad pushing tumor front

ii) WPOI-II: finger-like pushing pattern of tumor invasion

iii) WPOI-III: tumor islands having > 15 cells (large tumor islands)

iv) WPOI-IV: tumor islands having < 15 cells (small tumor islands)

v) WPOI-V: tumor satellites which are away from the main tumor by 1 mm.

The number of mitotic figures, the degree of pleomorphism, and the intracellular or extracellular keratin pearl production were the basis for histological grading. Well-differentiated tumors with a low degree of nuclear pleomorphism, keratinization or keratin pearl production, and intercellular desmosome connections in more than 75% of the tumor, with just sporadic mitotic figures. In tumors that are moderately differentiated, about 25% of the cells exhibit keratin pearl production

and intercellular connections, with sporadic mitotic figures/10 hpf. Tumor cells were classified as poorly differentiated SCC if they lacked keratinization, intercellular desmosome connections, and 10/10hpf mitotic patterns combined with noticeable pleomorphism.[12]

DOI was another histological parameter that was divided into two categories: a) up to 4 mm and b) >4 mm.[13]

To analyze and correlate WPOI with several clinicopathological characteristics, such as histological grade, tumor staging, PNI, LVI, nodal metastases, and DOI, all the information was tabulated.

The samples were divided into two groups for analysis. Of the 42 patients, group A comprised of patients with WPOI I-IV (n=14) and group B, had patients with WPOI-V only (n=28). The results were analyzed between the groups. The data were analyzed using the Statistical Package for Social Sciences (SPSS) software, version 25. It was manufactured by IBM in Chicago, USA. A p-value was determined to be statistically significant as one that was less than 0.05.

Numbers and percentages were used to display the category variables. However, the mean and standard deviation were employed to display the quantitative data. The results were subjected to the following statistical tests:

1. The qualitative variables were compared using the Chi-square test, and if any of the cells had an expected value less than 5 then Fisher's exact test was employed.
2. To find significant risk factors for WPO-V, univariate logistic regression was employed.

RESULTS

The research comprised 42 patients, in total of which 36 (85.7%) were males and 6 (14.3%) were females. The ratio of males to females was 6:1 as well as the mean age was 39.52±12.05 years (range: 23–70 years). With 30 cases (71.4%), buccal mucosa was the most frequent site, compared to the tongue (23.8%). In Table I, the specific histological features are displayed. The distribution of T stage showed T1-2 (4.8%), T2-10 (23.8%), T3-8 (19%) and T4-22 (52.4%). According to the histopathological differentiation of SCC, moderately differentiated was the most reported type (85.7%) followed by well-differentiated (9.5%) and poorly differentiated (4.8%) is the least reported type. Regarding the DOI, 85.7% were >4mm in depth and 14.3% were up to 4mm in depth. LVI and PNI were noted at 14.3% (n=6) and 57.1% (n=24) respectively. Concerning lymph node staging, a high proportion of the patients (47.6%, n=20) had N3 disease .

Table I: Descriptive characteristics of the patients

Variables	
Categories	
Age	**Mean±SD**
	39.52±12.05
Gender	**N (%)**
Male	36(85.7%)
Female	6(14.3%)
Histological grade	
Well differentiated	4 (9.5%)
Moderately differentiated	36 (85.7%)
Poorly differentiated	2 (4.8%)
Tumor site	
Buccal mucosa	30 (71.4%)
Tongue	10 (23.8%)
Maxillary alveolar process	2 (4.8%)
Depth of invasion	
Upto 4 mm	6 (14.3%)
>4mm	36 (85.7%)
Worst pattern of invasion	
I-IV	14 (33.3%)
V	28 (66.7%)
Lymphovascular invasion	
Present	6 (14.3%)
Absent	36 (85.7%)
Perineural invasion	
Present	24 (57.1%)
Absent	18 (42.9%)
Staging	
T1	2 (4.8%)
T2	10 (23.8%)
T3	8 (19%)
T4	22 (52.4%)
Nodal status	
N0	12 (28.6%)
N1	4 (9.5%)
N2a	4 (9.5%)
N2b	2 (4.8%)
N2c	0
N3	20 (47.6%)

The association between WPOI and demographic characteristics has been shown in Table II and a significant association has been found between WPOI with age (0.000) and WPOI with tumor site (0.005).

Histopathological features and WPOI:

Table II: Association between WPOI with demographic characteristics

Demographic characteristics	WPOI (I -IV)	WPOI (V)	Total	*p*-value
Age	14	28	42	
Mean±SD				0.000 *
39.52±12.05				
Gender				
Male	12	24	36	1.000
Female	2	4	6	
Site of tumor				
Buccal mucosa	10	20	30	
Maxillar y alveol ar process	1	1	2	0.005 *
Tongue	4	6	10	

Fisher's exact test, p-value <0.05

Table III: Association between WPOI with histopathological characteristics

Pathological parameters	WPOI (I -IV)	WPOI (V)	Total	*p*-value
Histological grade #				
Well differentiated	1	3	4	
Moderately differentiated	12	24	36	0.009*
Poorly differentiated	1	1	2	
Depth of invasion #				
Upto 4mm	2	4	6	0.155
> 4mm	12	24	36	
Lymphovascular invasion#				
Identified	2	4	6	0.083
Not identified	12	24	36	
Perineural invasion				
Identified	8	16	24	0.000 *
Not identified	6	12	18	
Tumor staging#				
T1	1	1	2	
T2	4	6	10	0.000 *
T3	3	5	8	
T4	8	14	22	
Nodal status #				
N0	4	8	12	
N1	1	3	4	
N2a	1	3	4	0.348
N2b	1	1	2	
N2c	0	0	0	
N3	6	14	20	

Fisher's exact test, °Chi-square test, p-value <0.05 significant

POI was divided into two groups: non-infiltrative (POI-I to IV) and infiltrative (POI-V) and there was a correlation between the two groups using several histopathological criteria. 33.3% of patients (n=14) had WPOI I-IV whereas pattern V was found in 66.7% of the patients (n=28). Histological grade, PNI, and tumor stage were the histological factors that were significantly associated with WPOI, with p-values of 0.009, 0.000, and 0.000, respectively. However, for DOI, LVI and nodal status, the results were not significant (p- 0.155, 0.083 and 0.348 respectively) with WPOI (Table III).

In univariate analysis, a significant association of tumor staging (p=0.002) and PNI (P=0.001) has been found

Table IV: Univariate logistic regression to find out significant risk factors of WPOI-V

Variable	Beta coefficient	Standard error of mean	*p*-value	Odds ratio
Age (years)	0.049	0.032	0.126	1.050
Gender	0.000	0.935	1.000	1.000
Histologic grading	-20.247	28420.75	0.999	0.000
Depth of invasion	-1.649	0.943	0.080	0.192
Perineural invasion	3.091	0.892	0.001*	22.000
Lymphovascular invasion	20.751	16408.711	0.999	1028029459
Tumor staging	-3.401	1.103	0.002*	0.033
Lymph nodes	-0.847	1.113	0.446	0.429

(Table IV). No significant association was detected with age, gender, histologic grading, DOI, LVI and lymph nodes.

DISCUSSION

A primary critique of the TNM system is its disregard for the unique histological characteristics of tumors.[14] To help with this, several histological characteristics have been investigated and taken into account when making decisions on adjuvant treatment. There are several prognostic factors that could impact survival. One of these factors is the invasion pattern. It is defined as the invasive front of the tumor at the interface between the tumor and the host.[15]

In the past, numerous histological prognostic models and grading systems have been created to forecast the biological behavior of OSCC. POI continues to play a significant role in each of these systems of grading. Jakobsson et al. created a multifactorial grading system in 1973 that scored tumor-host interactions and tumor features, however, it ultimately only worked well for tongue tumors. A revision of Jakobsson's approach was later suggested by Anneroth et al., who did so by evaluating six histomorphological characteristics.[16] Anneroth's grading system was amended by Bryne, who created a malignancy grading system that solely considered the tumor's invasive front.[17] Brandwein has developed a risk assessment score that predicts survival and local recurrence by including PNI, invasion pattern, and lymphocyte response.[18]

The pattern of invasion is indicative of biological mechanisms of malignancy, including enhanced tumor cell motility, lack of contact inhibition, and proteolytic enzyme output. A straightforward indicator of tumor behavior is provided by its findings in standard histological preparations. According to molecular analysis of the invasion pattern, deep invasive tumor fronts exhibit more cyclin-B1 and Ki-67 markers while expressing less E-cadherin. Consequently, there is a greater chance that cancerous cells may spread.[19]

The most frequent location of primary tumor in our study was the buccal mucosa, which was followed by the tongue. De Silva et al. discovered that the tongue was the most often affected region in their retrospective analysis of 623 individuals with oral and tongue malignancies. They also discovered that the rate of occult nodal positivity was significantly greater in the tongue than in the buccal mucosa.[20] Nodal spread happens early and quickly because the tongue's anatomical location near the floor of the mouth provides it with a strong supply of lymphatics. The standard histological reporting format requires the use of several histological markers, including tumor stage, different histological grades, DOI, LVI, and PNI, which are well-known prognostic variables for OSCC in all stages. Lundqvist et al.[21] and Kane et al.[22] were among the few earlier studies that did not demonstrate a significant correlation between WPOI and nodal involvement, similar to our research which showed a *p*-value of 0.348. A reduced sample size could be the cause of the non-significant association.

By univariate analysis, the several histological characteristics that demonstrated a strong association with WPOI in our study included the presence of PNI (0.001) and tumor staging (0.002). Almangush et al. reported similar results, indicating that early stages of oral SCC were substantially correlated with WPOI IV-V.[23] Furthermore, Adil et al. reported a significant

association between WPOI and tumor stage, nodal involvement, histological grade, LVI, PNI, DOI and tumor budding.[24] Marzouki et al. emphasized the worst prognosis of oral SCC by comparing WPOI V to other histological markers and determining that it was an independent predictive element for local recurrences.[25] WPOI IV and V were identified by Binmadi et al. in a meta-analysis they conducted as predictors of local recurrence and nodal metastasis, as well as markers of poor outcomes such as lower overall and disease-free survival.[26]

There were drawbacks to the study in relation to follow-up with patients, hence a disease-free survival was not evaluated. Second, because the study was retrospective, the data interpretation was heavily reliant on what was recorded at the time of surgery and finally the research was performed in a single place, therefore, the findings need to be externally validated to justify broad practice adjustments.

CONCLUSION

We have found a significant association between WPOI and clinipathological characteristics in patients of OSCC. This study is among the few that have assessed the function of WPOI as a separate indicator of prognosis. In conclusion, the invasion pattern is a readily identifiable histological characteristic that has to be reported with oral SCCs regularly.

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SOURCE OF FUNDING: None

Authors' Contribution

Kanwal Iqbal: Conception of study / Designing / Planning, Analysis / Interpretation / Discussion, Manuscript Writing

Fizza Abidi: Conception of study / Designing / Planning, Critical Review

Zofeen Hashim Bhurgri: Experimentation / Study Conduction

Sana Fatima: Critical Review

REFERENCES

1. Purwanto DJ, Soedarsono N, Reuwpassa JO, Adisasmita AC, Ramli M, Djuwita R. The prevalence of oral high risk HPV infection in Indonesian oral squamous cell carcinoma patients. Oral diseases. 2020;26(1):72 80. DOI: 10.1111/odi.13221
2. Ferreira e Costa R, Leão ML, Sant'Ana MS, Mesquita RA, Gomez RS, Santos-Silva AR, et al. Oral squamous cell carcinoma frequency in young patients from referral centers around the world. Head and Neck Pathology. 2022;16(3):755-62. DOI: 10.1007/s12105-022-01441-w.
3. Givony S. Oral squamous cell carcinoma (OSCC) an overview. J Med Sci. 2020;8:67-74. [Available from: https://medicsciences.com/f/2020/ORAL-SQUAMOUS-CELL-CARCINOMA-OSCC-AN-OVERVIEW-shahaf-givony-2020.pdf]
4. Alqutub S, Alqutub A, Bakhshwin A, Mofti Z, Alqutub S, Alkhamesi AA, et al. Histopathological predictors of lymph node metastasis in oral cavity squamous cell carcinoma: a systematic review and meta-analysis. Frontiers in Oncology. 2024;14:1401211. DOI:10.3389/fonc.2024.1401211.
5. Verma R, Singh A, Chowdhury N, Joshi PP, Durgapal P, Rao S, et al. Evaluation of histomorphological parameters to predict occult nodal metastasis in early-stage oral squamous cell carcinoma. Turkish Journal of Pathology. 2022;38(3):227. DOI: 10.5146/tjpath.2021.01566.
6. Almangush A, Mäkitie AA, Triantafyllou A, de Bree R, Strojan P, Rinaldo A, et al. Staging and grading of oral squamous cell carcinoma: An update. Oral oncology. 2020;107:104799. DOI:10.1016/j.oraloncology.2020.104799.
7. Edition S, Edge S, Byrd D. AJCC cancer staging manual. AJCC cancer staging manual. 2017.
8. Chatterjee D, Bansal V, Malik V, Bhagat R, Punia RS, Handa U, et al. Tumor budding and worse pattern of invasion can predict nodal metastasis in oral cancers and associated with poor survival in early-stage tumors. Ear, Nose & Throat Journal. 2019;98(7):E112-9. DOI: 10.1177/0145561319848669.
9. Binmadi NO, Mohamed YA. Impact of worst pattern of invasion on prognosis of oral squamous cell carcinoma: a systematic review and meta-analysis. Journal of International Medical Research. 2023;51(10): 03000605231206260. DOI: 10.1177/03000605231206260.
10. Müller S, Boy SC, Day TA, Magliocca KR, Richardson MS, Sloan P, et al. Data set for the reporting of oral cavity carcinomas: explanations and recommendations of the guidelines from the international collaboration of cancer

reporting. Archives of pathology & laboratory medicine. 2019;143(4):439-46. DOI: 10.5858/arpa.2018-0411-SA.
11. Lakhera KK, Nama Y, Maan P, Jindal R, Patel P, Singh S, et al. Worst pattern of invasion as a predictor of nodal metastasis in early-stage oral squamous cell carcinoma. Indian Journal of Surgical Oncology. 2023;14(1):160-8. DOI: 10.1007/s13193-022-01639-y.
12. Lin NC, Hsu JT, Tsai KY. Survival and clinicopathological characteristics of different histological grades of oral cavity squamous cell carcinoma: A single-center retrospective study. PloS one. 2020;15(8):e0238103. DOI: 10.1371/journal.pone.0238103
13. Abidi F, Fatima S, Zaidi A, Butt S, Saeed S, Batool H. Depth of Invasion as Tumor Indicator in Cervical Lymph Node Metastasis in OSCC. Journal of Pharmaceutical Research International. 2022: 34(27A): 45-51. DOI: 10.9734/jpri/2022/v34i27A35993
14. Chiu K, Hosni A, Huang SH, Tong L, Xu W, Lu L, et al. The potential impact and usability of the eighth edition TNM staging classification in oral cavity cancer. Clinical Oncology. 2021;33(10):e442-9. doi.org/10.1016/j.clon.2021.05.007
15. Kim MJ, Ahn KM. Prognostic factors of oral squamous cell carcinoma: the importance of recurrence and pTNM stage. Maxillofacial Plastic and Reconstructive Surgery. 2024;46(1):8. DOI: 10.1186/s40902-024-00410-3.
16. Pandya JA, Natarajan S. A study on histological grading systems of oral squamous cell carcinoma and comparison of their efficacy in determining the nature (clinical and histopathological) and prognosis of oral squamous cell carcinoma. Journal of Cancer Research and Therapeutics. 2023;19(Suppl 1):S198-205. DOI: 10.4103/jcrt.JCRT_1641_20.
17. Chaware S, Mahajan A, Sangle V, Gajdhar S, Sarode S, Kendre S. Analysis of Histopathological Parameters of Oral Squamous Cell Carcinoma by Bryne's Grading in Different Age Groups. Journal of Clinical & Diagnostic Research. 2021;15(12). DOI: doi.org/10.7860/JCDR/2021/52297.15750
18. Akolkar S, Hande A, Patil SK, Sonone AM, Pakhale A. Assessment of Bone Invasion and Its Correlation With Brandwein-Gensler Criteria in Oral Squamous Cell Carcinoma. Cureus. 2024;16(5). DOI: 10.7759/cureus.61194
19. Mishra A, Das A, Dhal I, Shankar R, Bhavya BM, Singh N, et al. Worst pattern of invasion in oral squamous cell carcinoma is an independent prognostic factor. Journal of Oral Biology and Craniofacial Research. 2022;12(6):771-6. DOI: 10.1016/j.jobcr.2022.08.027
20. De Silva RK, Siriwardena BS, Samaranayaka A, Abeyasinghe WA, Tilakaratne WM. A model to predict nodal metastasis in patients with oral squamous cell carcinoma. PloS one. 2018;13(8):e0201755. doi.org/10.1371/journal.pone.0201755
21. Lundqvist L, Stenlund H, Laurell G, Nylander K. The importance of stromal inflammation in squamous cell carcinoma of the tongue. Journal of oral pathology & medicine. 2012;41(5):379-83. DOI: 10.1111/j.1600-0714.2011.01107.x.
22. Kane SV, Gupta M, Kakade AC, D'Cruz A. Depth of invasion is the most significant histological predictor of subclinical cervical lymph node metastasis in early squamous carcinomas of the oral cavity. European Journal of Surgical Oncology (EJSO). 2006;32(7):795-803. DOI: 10.1016/j.ejso.2006.05.004
23. Almangush A, Bello IO, Keski–Säntti H, Mäkinen LK, Kauppila JH, Pukkila M, et al. Depth of invasion, tumor budding, and worst pattern of invasion: prognostic indicators in early stage oral tongue cancer. Head & neck. 2014;36(6):811-8. DOI: 10.1002/hed.23380.
24. Khan AA, Ahuja S, Zaheer S, Mitha M, Ranga S. Association of worst pattern of invasion in oral squamous cell carcinoma with clinicopathological parameters. Journal of Medicine, Surgery, and Public Health. 2023;1:100029. doi.org/10.1016/j.glmedi.2023.100029
25. Marzouki HZ, Bukhari AF, Al-Ghamdi DA, Abdullah RM, Al-Hajeili M, Khayyat S, et al. Worst pattern of invasion and other histopathological features in oral cancer as determinants of prognosis and survival rate: a retrospective cohort analysis. Oncology letters. 2023;25(2):75. DOI: 10.3892/ol.2023.13661
26. Binmadi NO, Mohamed YA. Impact of worst pattern of invasion on prognosis of oral squamous cell carcinoma: a systematic review and meta-analysis. Journal of International Medical Research. 2023;51(10):03000605231206260. DOI: 10.1177/03000605231206260

RESEARCH ARTICLE

COMPARISON OF TEAR FILM DYSFUNCTION AFTER PHACOEMULSIFICATION BETWEEN DIABETICS AND NON-DIABETICS

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ABSTRACT

Objectives: *To compare early postoperative tear film break-up time (TBUT) after phacoemulsification between diabetic and non-diabetic cataract patients.*

Study design: *Quasi-experimental (comparative) study.*

Place and duration of study: *Ophthalmology Department, Fauji Foundation Hospital, Rawalpindi, Pakistan; July 2024 – September 2024.*

Patients and methods: *Sixty-six patients scheduled for phacoemulsification with intraocular lens implantation were enrolled by consecutive non-probability sampling: 33 long-standing diabetics (> 5 years) and 33 non-diabetics. Exclusion criteria included prior ocular surface disease, significant meibomian gland dysfunction, prior ocular surgery, topical ocular medication use, or complicated surgery. All surgeries used a 2.8 mm temporal clear corneal incision under topical anesthesia. TBUT was measured at slit lamp using fluorescein one day preoperatively and one day postoperatively. TBUT <10 s was considered abnormal. Statistical analysis employed paired-samples t-tests for within-group comparisons and independent-samples t-tests for between-group comparisons (SPSS v23); p<0.05 was considered significant.*

Results: *Mean preoperative TBUT did not differ between groups (diabetics 12.70±3.72 seconds; non-diabetics 12.79±3.65 seconds; p=0.92). Postoperatively, TBUT decreased in both groups, with a significantly greater reduction in diabetics (7.36±2.16 seconds) than non-diabetics (10.42±3.56 seconds) (p<0.01).*

Conclusion: *Diabetic patients experienced a significantly larger early postoperative decline in TBUT following phacoemulsification compared with non-diabetics. Consideration should be given to prophylactic or early postoperative lubricants for diabetic patients to mitigate dry-eye symptoms.*

Keywords: *Tear film break-up time, diabetic, dry eye, phacoemulsification*

INTRODUCTION

The tear film is an important part of the ocular anatomy. Not only does it serve as a source of nutrition and oxygen but also acts as a lubricant to the ocular surface, preventing it from drying and allowing the palpebral conjunctiva to easily slide over the cornea without causing any abrasive damage. Tears are vital for maintaining comfort, safeguarding against infections, controlling inflammation, facilitating the healing of trauma or surgery-related injuries, removing debris, and sustaining clear vision.[1] Problems arise, however, when there is inadequate tear production or excessive tear evaporation which may lead to dry eye symptoms manifested as dryness, discomfort, pain, a gritty sensation, blurry vision, redness, foreign-body sensation, and visual disturbances. These symptoms can greatly interfere with daily activities like reading, driving, and using screens or visual display devices.[2] Given the prevalence of dry eye syndrome, estimated at around 18.7% in Pakistan[3] and approximately 11.59% globally[4], this represents a significant issue that warrants careful attention and effective management.

Several factors can contribute to the onset of this condition. Cataract surgery is one such factor in which the clear corneal incision (CCI) made during the procedure compromises the integrity of the ocular surface, potentially leading to tear film dysfunction. Additionally, the prolonged use of preservative-

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containing topical medications after surgery can contribute to the development of dry eye symptoms. A large-scale systematic review concluded that 37.4% of patients with no dry eye disease developed it after cataract surgery.[5]

Another known risk factor for dry eye syndrome is diabetes. Persistent hyperglycemia leads to disrupted tear film dynamics and osmolarity, triggers the inflammatory cascade, and activate the innate immune response, which subsequently causes oxidative stress.[6] The prevalence of type 2 diabetes in Pakistan was estimated to be around 10% in a recent systematic review[7] which predisposes a large population to dry eye syndrome. Globally, approximately 541 million adults report having impaired glucose tolerance, a significant risk factor for developing type 2 diabetes.[8] The occurrence of dry eye has also been linked to glycated hemoglobin levels, with higher glycated hemoglobin levels being associated with a greater incidence of dry eye.[9] Many diabetic patients report symptoms such as a foreign body sensation and burning, which indicate possible tear film abnormalities.

Although dry eye is common after cataract surgery and diabetic patients are known to have tear film abnormalities, limited research has examined the combined impact of diabetes and phacoemulsification on early postoperative tear film stability. Understanding this relationship is important for guiding postoperative care and preventing ocular surface complications. This study was designed to compare early postoperative TBUT changes as an indicator of tear film dysfunction between diabetic and non-diabetic patients undergoing phacoemulsification with intraocular lens implantation..

PATIENTS AND METHODS

A quasi-experimental study involving 66 patients comprising 33 diabetics and 33 non-diabetics was conducted at Fauji Foundation Hospital Rawalpindi Pakistan from July 2024 to September 2024 following ethical approval (vide letter no. No. 852/RC/FFH/RWP dated: 20/06/2024). Patients who were scheduled to undergo cataract surgery were selected from the ophthalmology outpatient department via non-probability consecutive sampling. Patients who were known diabetics for at least 5 years and taking medication for it were included in the diabetic group and their blood glucose levels were monitored throughout the study. The study protocol, patient information sheet, and consent form were approved by the Institutional Ethics Committee. Informed consent was secured from all participants.

The exclusion criteria comprised a history of conjunctival or corneal disorders, significant meibomian gland dysfunction (MGD), prior eye surgeries, and any systemic conditions that might influence tear production. Furthermore, any patients who had a complicated surgery as well as patients already using any topical eye medications were also excluded.

All participants underwent phacoemulsification under topical anaesthesia using 0.5% proparacaine. A foldable intraocular lens was placed in the capsular bag via a 2.8 mm temporal clear corneal incision. Postoperatively, patients were prescribed moxifloxacin 0.5% and prednisolone acetate 1% every two hours for the first week. Oral mefenamic acid tablets were provided as needed for pain relief. Patients were assessed both preoperatively and on the first postoperative day, with evaluation including slit-lamp examination, corneal fluorescein staining, tear film assessment, and measurement of TBUT.

For the TBUT test, the patient was seated at the slit lamp. While the patient gazed upward, the lower eyelid was carefully retracted, and a moistened fluorescein strip was placed in the inferior fornix. The patient was asked to blink three times and then look straight ahead. The cornea was subsequently examined at low magnification with a cobalt blue filter on the slit-lamp microscope. The duration between the final blink and the emergence of the first dry spot on the cornea was noted. A TBUT of less than 10 seconds was deemed abnormal.

A paired samples t-test was conducted to assess the statistical significance of the difference in TBUT between the preoperative and postoperative measurements in both groups while independent samples t-test determined inter-group statistical significance of preoperative and postoperative TBUT. p-value was kept significant at <0.05. All data analyses were conducted using SPSS for Windows version 23.

RESULTS

A total of 33 diabetic and 33 non-diabetic patients participated in the study. Sixty-two of these were females while the remaining 4 were male. The ages of all subjects ranged from 44 to 79 with a mean of 62.86 ± 6.9. Among males the mean age was 68 ± 10.42 while among females it was 62.53 ± 6.62. Both groups showed a decrease in mean pre-op TBUT: diabetic patients had a mean pre-op TBUT of 12.70s ± 3.72 while the non-

diabetic patients' mean pre-op TBUT was 12.79s ±3.65. The p-value was 0.92. Mean post-op TBUT among diabetics was 7.36s ±2.16 while in non-diabetics the mean post-op TBUT was 10.42s ±3.56. The p-value was <0.01 indicating a significant difference in both groups.

Table 1: Comparison of Tear Film Break-Up Time (TBUT) in Diabetic and Non-Diabetic Patients Undergoing Phacoemulsification

Parameter	Non-diabetic n=33	Diabetic n=33	*p*-value
	Mean ± SD	Mean ± SD	
Pre-op TBUT (seconds)	12.79 ±3.65	12.70 ±3.72	0.92
Post-op TBUT (seconds)	10.42 ±3.56	7.36 ±2.16	<0.01

DISCUSSION

Multiple factors play a role in the development of dry eye after surgery. It is known that cataract surgery can lead to disruption of tear film due to a number of reasons as were described in a review article. These include corneal nerve severing, prolonged exposure to microscope lighting, the use of a speculum, and the heat produced by phacoemulsification devices.[10] The irritated ocular surface often accumulates chemical mediators, such as free radicals, cyclooxygenase and proteolytic enzymes due to inflammation. Moreover, the loss of goblet cells and dysfunction of the meibomian glands following cataract surgery can also lead to evaporative dry eye syndrome. Diabetes is also a known contributor to dry eye symptoms. It leads to epithelial barrier dysfunction, which in turn results in corneal complications and eventual lacrimal functional unit impairment.[11] The impaired epithelial barrier function has also been correlated with increased serum HbA1c levels.[11] Numerous corneal complications result from diabetes mellitus including epithelial defects and corneal ulcers which also cause DES.[12] Diabetic patients with peripheral neuropathy have been found to exhibit impaired corneal neurons and decreased corneal sensitivity.[13] Patients with diabetes have also been found to experience chronic tear secretion deficiency and tear film dysfunction.[14]

Both these factors have been extensively investigated in research however their combined effects have not been given the same regard. Increased incidence of dry eye symptoms in early postoperative period can be very harmful especially if it leads to constant eye rubbing by the patient, possibly resulting in wound leakage, iris prolapse and, in some cases, postoperative endophthalmitis. Therefore, for the prognosis of good vision any untoward symptoms need to be dealt with promptly. So far there have not been any general guidelines that cater to the needs of diabetic patients that may be predisposed to dry eye symptoms. If these symptoms can be forecasted then the harm, they may bring about in early postoperative period can be mitigated if appropriately managed.

There have been extensive studies that compare the tear film dysfunction of diabetics with non-diabetics using many parameters including TBUT, tear film height, Schirmer test and corneal staining. Literature however is deficient in describing the use of these parameters in figuring out the superadded effect of surgical interventions such as phacoemulsification and evaluating the compounded effect that it may result in.

It was reported in a study with 83 participants using various examination techniques that among diabetics Schirmer test and TBUT were reduced and higher grades of keratoepitheliopathy score and rose bengal staining were present as compared to non-diabetics while conjunctival impression cytology showed goblet cell loss and conjunctival squamous metaplasia among diabetics as compared to non-diabetics.[15] One study investigated the difference in tear film osmolar concentration as well as other tear film parameters in 51 diabetic patients and 20 non-diabetics to reveal a significantly increased tear film osmolarity among patients with increased HbA1c (>8%) and in patients with a longer duration of DM.[16] However, they also noted insignificantly lower Schirmer and TBUT scores among diabetics. Additionally, the outcomes of these tests were unaffected by the patients' glycemic control status. We noted a minor decrease in TBUT in diabetics with some variation in values.

Postoperative thickness of the lipid layer of the tear film is reported to correlate with duration of diabetes leading to significant thinning one month after surgery, resulting in subsequent dry eye symptoms.[17] According to a study the incidence of dry eye following phacoemulsification was 9.8% which was significant.[18] Another study found no significant association between factors like age, gender, place of residence, occupation, BMI, or the type of surgery (whether SICS or phacoemulsification) and the occurrence of dry eye at both 7 days and 1 month postoperatively but in the phacoemulsification group,

an exposure time exceeding 15 minutes was notably linked to a higher risk of dry eye at the first follow-up.[19] Our findings strongly suggest that there is a clear difference in reduction of TBUT of diabetics as compared to non-diabetics in early postoperative period. Since our results suggest that incidence of dry eye symptoms in the early post-operative period is quite high, we suggest including a topical lubricant while prescribing postoperative medication to diabetics. Postoperative use of diquafosol 3% was found to be superior to hyaluronic acid [20] and could be considered as an alternative to conventional topical lubricants for better outcome.

There were a number of limitations of our study. Since we only scrutinised the early postoperative period in all patients our study did not spread much light on the long-term outcome of dry eye symptoms of diabetics undergoing cataract surgery which we feel is important. The sample size, though adequate, could be enlarged for a better representation of the population. Other factors that may involve or affect tear film dysfunction should ideally also be factored in when investigating the tear film. Utilizing other parameters such as lipid layer thickness, in evaluating tear film dysfunction may also be of benefit.

CONCLUSION

Diabetic patients demonstrated a significantly greater postoperative reduction in TBUT compared with non-diabetics. Incorporating prophylactic or early postoperative topical lubricants such as dextran, hypromellose, or polyacrylic acid may help mitigate early dry-eye changes in diabetic individuals. Further studies assessing long-term postoperative outcomes in diabetics, including effects on TBUT, tear film osmolarity, and dry-eye symptom development, are warranted.

CONFLICT OF INTEREST

All authors state that they have no conflicts of interest.

ETHICAL STATEMENT

All subjects gave their informed consent for inclusion before they participated in the study. All procedures performed in this study involving human participants were conducted ethically according to the ethical standards of the Ethical Review Board of Fauji Foundation Hospital after awarding of the certificate of ethical approval (Ref No. 852/RC/FFH/RWP).

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Wali Waqar Qureshi: Conception of study/Designing/ Planning, Experimentation/Study Conduction, Analysis/Interpretation/Discussion, Manuscript Writing, Critical Review, Facilitated for Reagents/Material Analysis

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REFERENCES

1. Pflugfelder SC, Stern ME. Biological functions of tear film. Exp Eye Res. 2020;197:108115. DOI: 10.1016/j.exer.2020.108115
2. Tangmonkongvoragul C, Chokesuwattanaskul S, Khankaeo C, Punyasevee R, Nakkara L, Moolsan S, et al. Prevalence of symptomatic dry eye disease with associated risk factors among medical students at Chiang Mai University due to increased screen time and stress during COVID-19 pandemic. PLoS One. 2022;17(3):e0265733. DOI: 10.1371/journal.pone.0265733
3. Ayub A AF, Saleem N, Ali MH, Ayub MH, Butt NH. Frequency and Risk Factors of Dry Eye Disease in Pakistani Population, A Hospital Based Study. . Pak J Ophthalmol [Internet]. 2017;33(4). DOI: https://doi.org/10.36351/pjo.v33i4.26
4. Papas EB. The global prevalence of dry eye disease: A Bayesian view. Ophthalmic & physiological optics : the journal of the British College of Ophthalmic Opticians (Optometrists). 2021;41(6):1254-66. DOI: 10.1111/opo.12888
5. Miura M, Inomata T, Nakamura M, Sung J, Nagino K, Midorikawa-Inomata A, et al. Prevalence and Characteristics of Dry Eye Disease After Cataract Surgery: A Systematic Review and Meta-Analysis. Ophthalmology and therapy. 2022;11(4):1309-32. DOI: 10.1007/s40123-022-00513-y

6. Zhang X, Zhao L, Deng S, Sun X, Wang N. Dry Eye Syndrome in Patients with Diabetes Mellitus: Prevalence, Etiology, and Clinical Characteristics. J Ophthalmol. 2016;2016:8201053. DOI: 10.1155/2016/8201053
7. Umar Hasan S, Rehman Siddiqui MA. Nationwide prevalence of type 2 diabetes mellitus and pre-diabetes in Pakistan: A systematic review and meta-analysis. Diabetes Research and Clinical Practice. 2024;216. DOI: 10.1016/j.diabres.2024.111815
8. Cho NH, Shaw JE, Karuranga S, Huang Y, da Rocha Fernandes JD, Ohlrogge AW, et al. IDF Diabetes Atlas: Global estimates of diabetes prevalence for 2017 and projections for 2045. Diabetes Res Clin Pract. 2018;138:271-81. DOI: 10.1016/j.diabres.2018.02.023
9. Seifart U, Strempel I. [The dry eye and diabetes mellitus]. Der Ophthalmologe : Zeitschrift der Deutschen Ophthalmologischen Gesellschaft. 1994;91(2):235-9. PMID: 8012143
10. Sutu C, Fukuoka H, Afshari NA. Mechanisms and management of dry eye in cataract surgery patients. Curr Opin Ophthalmol. 2016;27(1):24-30. DOI: 10.1097/ICU.0000000000000227
11. Gekka M, Miyata K, Nagai Y, Nemoto S, Sameshima T, Tanabe T, et al. Corneal epithelial barrier function in diabetic patients. Cornea. 2004;23(1):35-7. DOI: 10.1097/00003226-200401000-00006
12. Ladea L, Zemba M, Calancea MI, Călțaru MV, Dragosloveanu CDM, Coroleucă R, et al. Corneal Epithelial Changes in Diabetic Patients: A Review. Int J Mol Sci. 2024; 25(6):3471. https://doi.org/10.3390/ijms25063471
13. Achtsidis V, Eleftheriadou I, Kozanidou E, Voumvourakis KI, Stamboulis E, Theodosiadis PG, et al. Dry eye syndrome in subjects with diabetes and association with neuropathy. Diabetes care. 2014;37(10):e210-1. DOI: 10.2337/dc14-0860
14. Goebbels M. Tear secretion and tear film function in insulin dependent diabetics. The British journal of ophthalmology. 2000;84(1):19-21. DOI: 10.1136/bjo.84.1.19
15. Kesarwani D, Rizvi SWA, Khan AA, Amitava AK, Vasenwala SM, Siddiqui Z. Tear film and ocular surface dysfunction in diabetes mellitus in an Indian population. Indian Journal of Ophthalmology. 2017;65(4):301-4. DOI: 10.4103/ijo.IJO_939_15
16. Derakhshan A, Abrishami M, Khajedaluee M, Omidtabrizi A, Moghaddam SG. Comparison between Tear Film Osmolar Concentration and Other Tear Film Function Parameters in Patients with Diabetes Mellitus. Korean J Ophthalmol. 2019;33(4):326-32. DOI: 10.3341/kjo.2013.0146
17. Zhang K, Zhang S, Yu J, Lu Y, Zhu X. Changes of the tear film lipid layer thickness after cataract surgery in patients with diabetes mellitus. Acta Ophthalmologica. 2021;99(2):e202-e8. DOI: 10.1111/aos.14565
18. Kasetsuwan N, Satitpitakul V, Changul T, Jariyakosol S. Incidence and pattern of dry eye after cataract surgery. PLoS One. 2013;8(11):e78657. DOI: 10.1371/journal.pone.0078657
19. Garg P, Gupta A. Dry eye disease after cataract surgery: study of its determinants and risk factors. Turk J Ophthalmol. 2020;50(3):133–42. DOI:10.4274/tjo.galenos.2019.45538
20. Kim S, Shin J, Lee JE. A randomised, prospective study of the effects of 3% diquafosol on ocular surface following cataract surgery. Scientific Reports. 2021;11(1):9124. DOI: 10.1016/j.aopr.2022.100063

RESEARCH ARTICLE

EVALUATION OF A NEW GLUCOMETER COMPARED TO A TRUSTED LAB METHOD: IMPROVING ACCURACY IN DIABETES MONITORING

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ABSTRACT

Objective: *Accurate blood glucose monitoring is vital for effective diabetes management, as it guides treatment decisions and helps prevent complications.*

Study design: *The aim of this study was to evaluate the accuracy and reliability of a new personal glucometer, MedSenso (MS) by comparing its glucose readings with those from the standard Cobas Pro laboratory analyzer.*

Place and duration of study: *The multicentered study was conducted at Islamabad Diagnostic Center Pakistan, from Nov 2024 to Mar 2025 after ethical approval.*

Patients and Methods: *We tested 200 venous blood samples from diabetic patients using both devices.*

Results: *The results demonstrated a strong correlation between MedSenso and Cobas Pro, with a Pearson correlation coefficient of r = 0.978. The Cobas Pro measured an average glucose level of 208.40 mg/dL, while MedSenso showed a slightly lower average of 198.06 mg/dL. The standard deviations were 90.27 mg/dL and 85.33 mg/dL respectively, indicating slightly more consistent readings from MedSenso. Bland–Altman analysis showed that the differences between devices were small and within clinically acceptable limits, suggesting that the variation is unlikely to impact routine patient care.*

Conclusion: *Current study suggest that MedSenso provides comparable glucose measurements with those of Cobas Pro and reliable tool for point-of-care monitoring in clinical and home settings.*

Keywords: *Blood Glucose Monitoring, Cobas Pro, Diabetes Mellitus, MedSenso Glucometer, Point-of-Care Testing, Venous Blood*

INTRODUCTION

Diabetes mellitus is rapidly becoming one of the most significant global health challenges. According to the Global Burden of Disease (GBD) Study 2021 published by the University of Washington in *The Lancet*, approximately 537 million adults aged 20 to 79 were living with diabetes worldwide in 2021. This number is projected to increase to 643 million by 2030 and reach as high as 784 million by 2045, highlighting a substantial and ongoing rise in diabetes prevalence globally.[1,2]

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Diabetes is not only characterized by elevated blood glucose levels but is also associated with serious long-term complications, including cardiovascular disease, nephropathy, retinopathy, neuropathy, and an increased risk of limb amputations. These complications pose a considerable burden not only on individuals affected but also on healthcare systems worldwide, increasing both the demand for care and economic costs.

In Pakistan, the situation is particularly concerning. Recent estimates suggest that over 26 million adults are living with diabetes, making Pakistan one of the countries with the highest diabetes prevalence in South Asia.[2,3] Factors such as urbanization, sedentary lifestyles, dietary changes, and genetic predisposition contribute to this growing epidemic. The healthcare

infrastructure faces significant challenges in providing widespread diabetes screening and management, especially in rural and underserved areas. This makes the availability of reliable, easy-to-use, and affordable glucose monitoring devices critically important to improve early diagnosis and ongoing management of diabetes in the country.[4,5]

Blood glucose levels are categorized to guide diagnosis and management. Normal fasting blood glucose is defined as less than 100 mg/dL (5.6 mmol/L). Prediabetes is identified when fasting glucose ranges between 100 and 125 mg/dL (5.6 to 6.9 mmol/L), indicating impaired glucose regulation and a higher risk for developing type 2 diabetes. Diabetes is diagnosed when fasting glucose levels are 126 mg/dL (7.0 mmol/L) or higher on two separate occasions or when random glucose exceeds 200 mg/dL (11.1 mmol/L) in the presence of symptoms.[3,6-8] Maintaining glucose levels within the normal range is essential to prevent complications and improve quality of life.[9]

The increasing development of new medical devices underscores the need for thorough validation studies to verify their clinical accuracy and reliability in real-world settings. Understanding the capabilities and limitations of such devices assists patients, clinicians, and healthcare systems in adopting technologies that improve diabetes care. The findings from this study offer valuable insight into the utility of the MedSenso glucometer as a potential tool to enhance diabetes monitoring, especially in resource-limited clinics or home environments where access to full laboratory facilities is restricted.[3,4,5,10] We anticipate that these results will encourage wider adoption of patient-friendly devices that facilitate more accurate and convenient blood glucose monitoring, ultimately contributing to better diabetes control and outcomes.[6,11]

For comparison, we used the *Cobas Pro analyzer* (Roche Diagnostics), a laboratory-grade glucose measurement system widely regarded as a gold standard in clinical chemistry. It requires venous blood samples and is primarily used in hospital and laboratory environments.[5,9] By comparing MedSenso to Cobas Pro, this study aimed to assess whether the new glucometer could provide reliable glucose readings close to those from a trusted laboratory instrument, thereby offering a practical alternative for everyday diabetes management. In this study, we evaluated the performance of the MedSenso glucometer, a newly developed point-of-care blood glucose monitoring device designed for use in both clinical and home settings.

MATERIALS AND METHODS

This was a cross-sectional study conducted between November 2024 and March 2025 at the Islamabad Diagnostic Center (IDC), Pakistan, which operates over 120 branches nationwide, following approval from the Institutional Ethics Review Committee (approval number: ERBIDC21202505-ERC). The study was conducted in collaboration with the International Center of Medical Sciences Research (ICMSR), Islamabad, and the Army Medical College, Rawalpindi.

Participant Selection

A total of 200 adult participants previously diagnosed with either type 1 or type 2 diabetes mellitus were enrolled using a convenient non-random sampling method. Eligibility criteria included individuals aged 18 years or older who provided written informed consent. Exclusion criteria included individuals with known hematological disorders, severe anemia, or those who had recently received blood transfusions, as these conditions could interfere with the accuracy of glucose readings.

Ethical Considerations

All participants were fully informed about the purpose, procedures, risks, and benefits of the study. Written informed consent was obtained from each participant before enrollment. The study protocol was reviewed and approved by the institutional ethics board, and strict confidentiality of personal data was maintained throughout.

Device Under Evaluation

The MedSenso utilizes electrochemical biosensor technology, where glucose oxidase catalyzes the oxidation of glucose, generating an electrical signal proportional to the glucose concentration. Key features of the device include a minimal sample volume (~0.5 µL), rapid testing time (~5 seconds), and portability, making it suitable for both clinical and home use.

Reference Standard

The Cobas Pro Analyzer (Roche Diagnostics) was used as the reference laboratory standard. This high-precision device employs enzymatic colorimetric methods and integrates automated internal quality control systems to ensure accurate plasma glucose measurements. It requires venous blood samples and is widely regarded as a gold standard in clinical diagnostics.

Sample Collection and Handling

Blood samples were drawn by trained medical personnel using aseptic techniques. Venous blood was collected in sodium fluoride-containing tubes, which preserve glucose stability. Each sample was labeled and stored in temperature-controlled containers until analysis to maintain sample integrity.

Measurement and Analysis Protocol

Each sample was tested using both the MedSenso glucometer and the Cobas Pro Analyzer. Devices were calibrated and operated strictly according to the manufacturers' instructions.[4,5] Quality control procedures were rigorously followed, including the use of certified control materials and routine recalibration of equipment. Additionally, a subset of samples was retested to ensure consistency and accuracy. Any discrepancies were analyzed and resolved through comparison and re-evaluation.

Quality Assurance Measures

To maintain data validity and reliability, comprehensive quality assurance protocols were implemented. Both devices underwent regular maintenance and performance verification, and any deviations were immediately addressed. All analytical procedures were conducted in a standardized clinical laboratory environment, ensuring adherence to best laboratory practices.

RESULTS

Overall, the results demonstrated a strong linear correlation between the MedSenso and Cobas Pro devices, with a Pearson correlation coefficient of 0.978, indicating that the two methods generally tracked glucose variations in parallel. The average glucose measured by Cobas Pro was 208.40 mg/dL, compared to 198.06 mg/dL by MedSenso, with respective standard deviations of 90.27 mg/dL and 85.33 mg/dL. These small differences suggest that, on average, MedSenso provides readings consistent with the laboratory standard and with slightly less variability.

However, closer examination revealed several individual samples with relatively large discrepancies between the two devices. Notably, samples 22, 153, 160, and 198 exhibited differences exceeding 20 mg/dL. For example, sample 22 showed a difference of 24 mg/dL (Cobas Pro: 240 mg/dL vs. MedSenso: 216 mg/dL), while sample 160 had a 27 mg/dL discrepancy (Cobas Pro: 185 mg/dL vs. MedSenso: 158 mg/dL). These outliers may be attributed to factors such as sample handling variability, hematocrit interference, or intrinsic device limitations under certain physiological conditions. Despite these occasional larger differences, the overall agreement remained within clinically acceptable limits for routine glucose monitoring.

To further clarify the distribution of differences, Table I categorizes all 200 samples by the absolute difference between devices into four groups: differences of $\geqslant$ 10 mg/dL, $\geqslant$ 15 mg/dL, and $\geqslant$ 20 mg/dL. Of the total samples, 36 (18%) showed a difference of 10 mg/dL or more, 15 (7.5%) had differences of 15 mg/dL or more, and only 6 (3%) exceeded a difference of 20 mg/dL. These findings indicate that large discrepancies are infrequent and that most readings fall well within an acceptable margin of error for everyday clinical use.

Table I: Number of samples by absolute glucose difference between MedSenso and Cobas Pro

Difference Range (mg/dL)	Number of Samples	Percentage of Total (%)
≥10	36	18
≥15	15	7.5
≥20	6	3

In clinical practice, such minor differences are unlikely to alter therapeutic decisions, particularly when patients use the same device consistently for self-monitoring. Nonetheless, for cases where highly precise glucose values are critical, such as insulin dose adjustments in hospital settings, confirmation with a laboratory analyzer remains advisable.

DISCUSSION

Accurate blood glucose monitoring is a cornerstone of effective diabetes management, and the reliability of glucometers plays a crucial role in ensuring patient safety and optimal therapeutic outcomes. Numerous studies have evaluated the accuracy of various glucometers in comparison with laboratory-grade analyzers, consistently highlighting the variability in performance among commercially available devices. For instance, studies by Smith et al.[10] Zhang et al.[11], and Kumar and colleagues[12] demonstrated correlation coefficients ranging from 0.90 to 0.98 when comparing portable glucometers against standard lab systems, with many devices showing acceptable clinical accuracy but occasional significant discrepancies. Our findings with the MedSenso glucometer, which yielded a Pearson correlation coefficient of 0.978 compared to the Cobas Pro analyzer, align well with these published data,

confirming MedSenso's competitive performance in real-world clinical settings.

In contrast, some lower-cost glucometers on the market have been reported to produce less reliable results, particularly at extreme glucose concentrations or under conditions of altered hematocrit, which can lead to dangerous clinical consequences.[13,14] The high level of agreement observed in our study suggests that MedSenso offers accuracy on par with higher-end devices, making it a trustworthy choice for both patients and healthcare providers.

From an economic perspective, the affordability of glucose monitoring devices is a critical factor influencing accessibility and adherence, especially in low- and middle-income countries like Pakistan, where diabetes prevalence is rapidly rising.[15] The MedSenso glucometer is priced competitively, with an approximate upfront cost of $30 USD per device and a per-test strip cost of approximately $0.50 USD. This positions it favorably against many popular glucometers, whose prices range from $25 to $50 USD for the device and $0.60 to $1.20 USD per test strip.[16,17] By offering comparable accuracy at a lower cost per test, MedSenso may improve affordability and encourage more consistent glucose monitoring among diabetic patients.

Furthermore, the ease of use and quick result turnaround time provided by MedSenso enhances its suitability for both clinical and home settings, addressing a significant barrier in diabetes self-care adherence. While laboratory analyzers like the Cobas Pro remain the gold standard, their higher costs, need for trained personnel, and longer processing times limit their accessibility outside specialized centers.

As diabetes becomes more common worldwide, accurate and affordable monitoring tools are more important than ever. Our results showed that MedSenso's performance closely matched that of the lab analyzer, supporting the idea that effective monitoring doesn't have to be expensive or limited to labs. This is especially important in places with fewer resources. Although people may choose glucometers based on what's available in their country or what brand they trust, the need for accuracy is universal. The very high correlation seen in this study (0.978) shows that MedSenso is not just an option, it's a strong contender in the glucose monitoring space. It's accurate enough for use in a wide range of healthcare settings.[10,11,12]

Most importantly, this study shows that innovation can bring lab-level accuracy into more hands. MedSenso proves that precision doesn't have to stay in the lab, it can become part of everyday care at home or in the clinic.

CONCLUSION

These findings suggest that MedSenso provides glucose measurements comparable to those of a laboratory-grade analyzer. Given its ease of use and rapid results, MedSenso could be a dependable tool for point-of-care monitoring in clinics and home settings. However, laboratory confirmation is recommended when highly precise glucose values are critical for clinical decisions.

CONFLICT OF INTEREST:

None.

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REFERENCES

1. GBD 2021 Diabetes Collaborators. Global, regional, and national burden of diabetes from 1990 to 2021, with projections to 2050. Lancet. 2023;402(10397):203-234. DOI: 10.1016/S0140-6736(23)02044-5.
2. Basit A, Fawwad A, Qureshi H, Shera AS; NDSP Members. Prevalence of diabetes, pre-diabetes and associated risk factors: second National Diabetes Survey of Pakistan (NDSP), 2016-2017. BMJ Open. 2018 Aug 5;8(8):e020961. DOI: 10.1136/bmjopen-2017-020961.
3. American Diabetes Association. Classification and diagnosis of diabetes: standards of medical care in diabetes, 2023. Diabetes Care. 2023;46(Suppl 1):S19-S40. https://doi.org/10.2337/dc23-S002
4. MedSenso Healthcare Ltd. MedSenso Device Technical Manual. 2023.
5. Roche Diagnostics. Cobas Pro Analyzer User Guide. 2022.
6. World Health Organization. Use of point-of-care devices for diabetes management: a global perspective. WHO Technical Report. 2021.
7. International Diabetes Federation. Diabetes Atlas. Diabetes around the world in 2021. Available from: https://diabetesatlas.org/
8. Sun H, Saeedi P, Karuranga S, Pinkepank M, Ogurtsova K, Duncan BB, et al. IDF Diabetes Atlas: global and regional diabetes prevalence estimates for 2021. Diabetes Res Clin Pract. 2022;183:109119. DOI:10.1016/j.diabres.2021.109119
9. Leipheimer JM, Balter ML, Chen AI, Pantin EJ, Davidovich AE, Labazzo KS, et al. First-in-human evaluation of a hand-held automated venipuncture device. Technology. 2019;7(3-4):98-107. DOI: 10.1142/S2339547819500067.
10. Sapra A, Bhandari P. Diabetes. In: StatPearls. Treasure Island, FL: StatPearls Publishing; 2023.
11. Goez-Mora JE, Arbeláez-Córdoba N, Balcazar-Morales N, Rivadeneira PS. A concept for human use of real-time and remote monitoring of diabetic subjects using intermittent scanned continuous glucose measurement. Biomed Eng Online. 2024 Feb 28;23(1):26. DOI: 10.1186/s12938-024-01217-z.
12. Armocida B, Monasta L, Sawyer SM, Bustreo F, Onder G, Castelpietra G, et al. Burden of type 1 and type 2 diabetes among adolescents in 24 Western European countries, 1990–2019. Int J Public Health. 2024;68:1606491. DOI: 10.3389/ijph.2023.1606491.
13. Khadilkar KS, Bandgar T, Shivane V, Lila A, Shah N. Current concepts in blood glucose monitoring. Indian J Endocrinol Metab. 2013;17(S3):S643-S649. DOI: 10.4103/2230-8210.123556.
14. Aykal G, Yegin A, Tekeli Ö, Yilmaz N. A model for managing and monitoring the quality of glucometers used in a high-volume clinical setting. Biochem Med (Zagreb). 2016;26(2):202-9. DOI: 10.11613/BM.2016.022.
15. Kim SK, Suh S, Kim MY, Chung HS, Hur KY, Kim SW, et al. Three-day continuous glucose monitoring for hypoglycemic event assessment in type 1 diabetes. Endocr J. 2011;58(7):535-541. DOI: 10.1507/endocrj.k10e-378.
16. Gribovschi M. Methodology of glucose monitoring in type 2 diabetes mellitus. Clujul Med. 2013;86(2):93-96.
17. Zavalkoff SR, Polychronakos C. Evaluation of conventional blood glucose monitoring vs continuous subcutaneous sensor. Diabetes Care. 2002;25(9):1603-1606. DOI: 10.2337/diacare.25.9.1603.

REVIEW ARTICLE

A NARRATIVE REVIEW ON MICROENCAPSULATION: TECHNIQUES AND CLINICAL ASPECTS

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ABSTRACT

Microencapsulation technique is a process of converting solid, liquid and gases into microcapsules by using various processing techniques. It is used in pharmaceutical, food and agriculture industries. Microencapsulation technique shows broad potential opportunities for resolving important clinical problems by various drug targeting strategies; therefore, aim of current review is to summarize all published studies pertaining to different types of drug delivery system based on microencapsulation. This is a narrative review conducted from the literature from 2009 to 2024. More than 40 articles were downloaded. After abstracting related data, checking quality of data, it is presented in form of PRISMA flow diagram. Most practical microencapsulation techniques and their outcomes; solvent-evaporation method for immiscible phases, fluid-bed/air-suspension coating for taste-masking and linear release of modified-release drugs, phase-separation/coacervation method for desired particle-size for encapsulation, polymeric method, spraying-drying for appropriate particle-size, hot-melt method for taste-masking and maintaining structure of crystals. Clinical benefits accomplished by this technique are; ibuprofen and clarithromycin by taste-masking, fenretinide by enhancing solubility, diclofenac sodium by reducing side-effects, retinol by reduction of toxicity, omeprazole by oral route stability.

Drug development by microencapsulation technique is having wide ranging beneficial clinical implications in terms of superiority for uniformity, bioavailability, toxicity, stability and patient acceptance.

Keywords: *Microencapsulation; pharmaceutical; taste masking; fluid-bed coating; coacervation; spray drying; hot melt*

INTRODUCTION

Microencapsulation is a process by which tiny particles or droplets surrounded by thin coating and converted into microcapsules.[1] In this technique active ingredient is enclosed in a protective layer.[2] The ingredients (polymers) used for microencapsulation of different products are biocompatible and biodegradable.[3] Such characteristics of natural and synthetic polymers avoid the chances of any toxicity in the body.[4] It provides protection from the environmental factors by encapsulating reactive, sensitive and volatile substances[5] thus microencapsulation improves stability of encapsulated material. Microencapsulation have point of focus from pharmaceutical, nutraceutical, cosmetic and food industry due its ability for protection from degradation, interaction with biological environment and improve absorption.[6] Microencapsulation can be used to modify release of drug substance from pharmaceutical dosage form.[7] Targeted and controlled release drug delivery minimize the unwanted effects.[8] Most crucial phase of microencapsulation is selection of a core material. The selection of material is a determination factor in encapsulation and stability of the targeted product. As a core wall materials; carbohydrates, protein and lipids are generally used alone or in combination to form cover around core material.[9] Additionally with above material

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ethyl cellulose, melamine resin shell, epoxy resins are also used for sustained release behavior.[6]

Oral route of drug administration is most acceptable due to its non-invasiveness and convenience. Taste of the drug substance taken orally is the key factor for evaluation of organoleptic quality of drug dosage form.[10] Unpleasant taste adversely affects patient's adherence to treatment.[11] Various techniques for taste masking have been developed including; addition of sweetener and flavors; however, microencapsulation mask the undesirable taste of different pharmaceutical and nutraceutical products by encapsulating the drug substance and convert it into tasteless product.[12] Microencapsulation is also intended for sustained release drug delivery. Various types of natural and synthetic polymers are used for sustained release activity; which includes a biocompatible and biodegradable polymer such as Poly (lactide-co-glycolide).[4] Sustained release micro pellets not only reduce the frequency of drug administration and adverse effect but also maintain a steady drug plasma concentration.[4]

Stability of a drug product is a critical aspect for development of pharmaceutical dosage form; it ensures efficacy and safety of medication. Maintenance of drug stability under storage condition and human body is a challenge for formulation scientist. Chemical degradation of acid labile products like proton pump inhibitors takes place when taken orally.[13] The degradation produces toxic by-products and also reduce therapeutic efficacy.[14] The stability issue of acid labile products can be overcome by gastric-resistance microencapsulation.[14]

Importance of microencapsulation:

i) Protection from deteriorating effects of environmental factors.[15]

ii) Evaporation protection of volatile components.[16]

iii) Masking of undesirable odor and taste of products.[10,12]

iv) Achieving the desired rate for release of drug substance at targeted site.[4]

v) Improving drug stability and protection from degradation due to acidic pH of human stomach.[13]

Microencapsulation techniques: There are various microencapsulation techniques available:-

i. Solvent evaporation method.[17] Selection of this procedure depends on the properties of material to be encapsulated. Such as water soluble products; the most suitable procedure is double emulsion type, in which liquid phase containing substance entrapped into water insoluble matrix. Formation of emulsion occurs when aqueous solution containing soluble compound dispersed in dissolved polymer containing organic solvent. This emulsion then dispersed into another secondary aqueous solution; commonly known as W/O/W double emulsion. Due to this process aqueous solution entrapped into polymer and polymer appears as spherical due to secondary emulsion. Produced microspheres are stabilized by surfactant and hardened by continuous stirring to evaporate organic solvent.[17]

ii. Fluid bed coating /Air suspension coating. Fluidized bed coating techniques is used to apply a thin layer coating on surface of granules, pellets, crystal or powder to encapsulate it.[18] Encapsulated material can be taste masked and modify its release. This modification target is achieved through formulation of coating material. In this microencapsulation process three types of coating processes can be applied. These include fluidized bed top spray coating, fluidized bed bottom spray coating and fluidized bed tangential spray coating.[19]

iii. Phase separation/Coacervation method.[20] This process involves the separation of a liquid phase of coating material from a polymeric phase; wrapping in the form of uniform layer around the suspended particles.[20]

iv. Spray drying.[21] A microencapsulation process used for encapsulation of volatile compounds such as essential oils, flavors. Spray drying involved atomization of emulsion in moderate temperature drying area; where immediate evaporation of solvent occur living the essential oils entrapped in microcapsule.[21]

v. Hot-melt.[22] Microencapsulation by hot-melt involves the process of introducing mixture of active ingredient and thermoplastic polymers. Plasticizers are used along with active and thermoplastic polymers to reduce glass transition temperature.[22]

Clinical Application of Microencapsulated pharmaceutical products:

Microencapsulation has significantly improved pharmacokinetic properties of drugs. In certain drugs it is observed from literature that by this technique scientists improved pharmacokinetic behavior of drug and decreased minimum effective concentration.[23] It

also resolved many issues related to dosage which we are currently facing.[24] Now extensive research has been started on pharmaceutical products for improving patient compliance and pharmacokinetic properties of drugs. Here are some drugs reported in literature on which successful trials have been conducted.

i. Ibuprofen the most commonly used analgesic have been microencapsulated to resolve the issue of its intake and dosage through oral route.[24]

ii. Microencapsulated adipose tissues derived from mesenchymal cells have been successfully used for treatment of osteoarthritis, without immunosuppressant drugs.[25]

iii. Fenretinide have been evaluated for increasing its solubility for oral cancer chemo-preventive application for future.[26]

iv. To improve stability and achieve maximum antioxidant effect of Moringa oleifera L extract, successful microencapsulation has been achieved. Microencapsulation protected the leaf extract from environmental factors.[27]

v. Thymoquinone is the active ingredient present in black seed oil and have many therapeutic effects. To mask the bitter and unpleasant taste of thymoquinone microencapsulation of black seed oil has been achieved successfully.[28]

vi. Microencapsulation of diclofenac sodium have been performed. It is important for prevention of ulceration associated with its administration.[29]

vii. Modified release pellets of omeprazole for oral liquid dosage form is another milestone for patient with swallowing impairment. This microencapsulated product resist against gastric degradation and released in intestine. These liquid products remain intact for 10 days after reconstitution.[30]

Current and future trends in microencapsulation:

Microencapsulation formulated products have many advantages over normally formulated products. Used materials for microencapsulation are biocompatible and biodegradable.[31] Microencapsulation could bring improvement in pharmaceutical current approaches for various disease treatments. It is hope in near future, numerous studies of microencapsulation techniques are believed to result in the development of new and effective clinical protocols.[32]

The main aim of current review is to summarize all published studies pertaining to different types of drug delivery system based on microencapsulation. Microencapsulation technique shows broad potential opportunities for resolving important clinical problems by various drug targeting strategies.[33]

MATERIALS AND METHODS

In order to write current narrative review on microencapsulation, an orderly literature survey has been conducted from 2009 to 2023 by two authors. To collect the relevant data, title and key word technique were used for collection of appropriate literature.

Literature Search Strategy: Data have been collected from Research gate, science direct, springer links, IOP Science, International Journal of Pharmaceutical and Biomedical Science, Journal of Pharmaceutical Science and Research, Polish Pharmaceutical Society and Google scholar. Key words and truncation technique was used for the collection of relevant literature. Fifty articles were downloaded on microencapsulation. The articles selected after abstracting were forty having relevant information, quality and data; further synthesize and presented by PRISMA diagram (Fig. 1).[34] Initial screening was done by two authors and final eligibility was also checked by two authors after reading details of full text of selected literature. Technicalities of article were checked by one author and final check of all data was done by one author. The PRISMA diagram details how studies were identified, the results of abstract screening, the results of full text eligibility assessment; a breakdown of reasons for exclusion, and details of included studies. Full-text eligible articles were forty. All the articles were evaluated for their quality; type of journal, data collection methods, statistical tests, significance values, and interpretations made.

Quality of Literature Evaluation:

GRADE (Grading of Recommendation Assessment, Development and Evaluation) criteria were employed for establishing the quality of literature.[35] GRADE is an explicit and transparent system for decision-making regarding the best available literature. The quality of literature by GRADE criteria can be determined by the risk of bias, imprecision, inconsistency, indirectness, publication bias and large magnitude of effect, dose response gradients, and residual confounding in the published and non-published literature.[36]

Evidence/Literature Inclusion Criteria: Evidences about types of microencapsulation and clinical application in Literature published from 2009 to 2023.

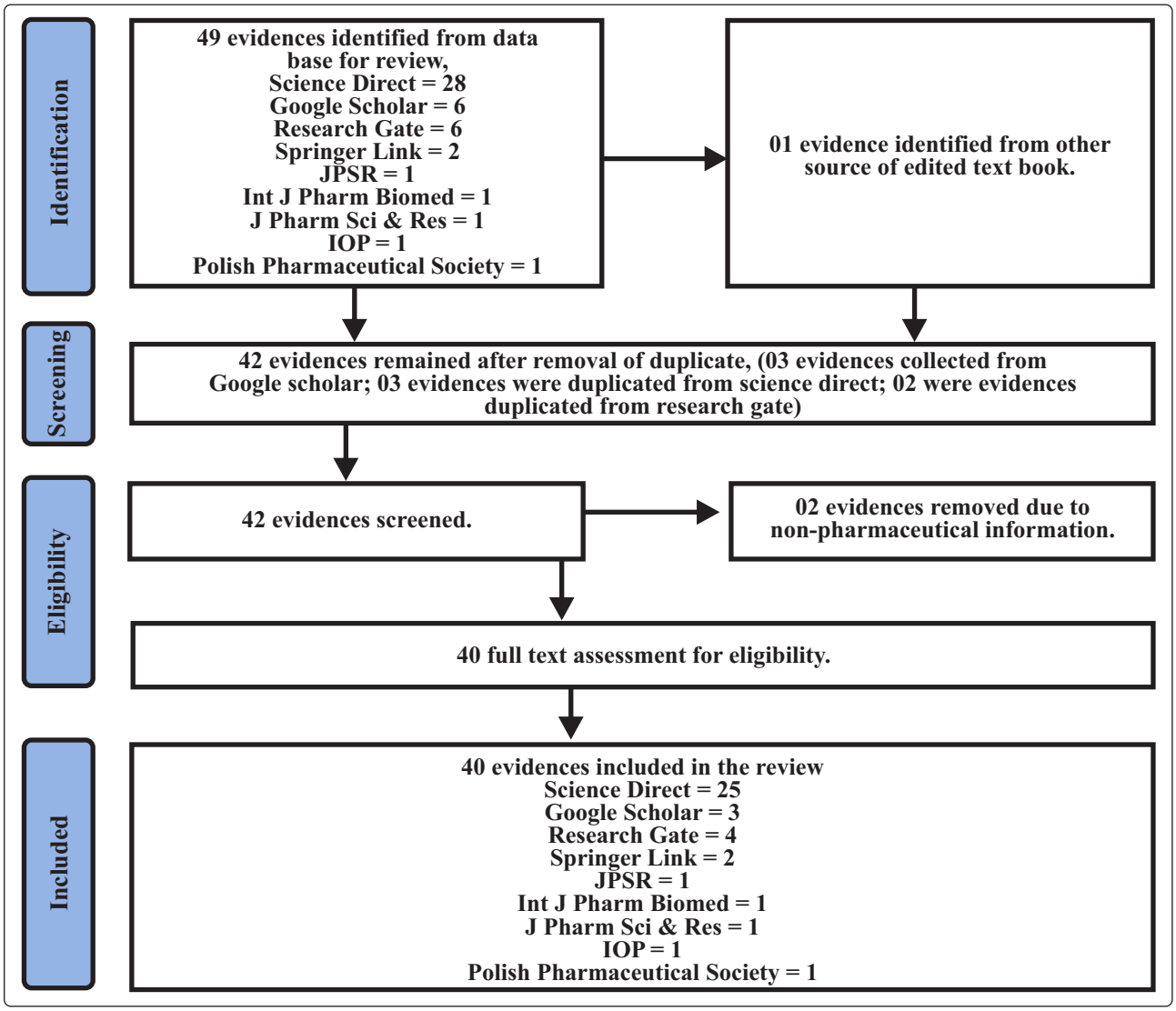

Figure 1: PRISMA

Evidence/Literature Exclusion Criteria: Literature reported with the microencapsulation techniques having data related to fertilizers and duplicates were excluded.

RESULTS

Review and literature assessment revealed most practical microencapsulation techniques and their outcomes. (Table I)

The clinical and pharmaceutical benefits e.g. pharmacokinetics, patient compliance and product stability have been achieved by using different microencapsulation techniques. (Table II)

DISCUSSION

Oxygen supply is essential for metabolic functions of living cells.[37] Oxygen supply through chemical means e.g. by hydrogen per oxide (H_2O_2) or naturally are key factors for the growth inhibitions of many anaerobic micro-organisms and thus wound healing.[37] Microencapsulation of gases is a challenging task for formulator but the solvent evaporation technique using poly (methyl methacrylate) solved that issue and successful, stable product can be achieved.[37] Similarly, microencapsulation technique of fluid bed coating have resolved many challenges encountering during the development of effective pharmaceutical formulations.[38] Drug solubility is a major challenge for the development of effective product; especially for the drugs having low intrinsic solubility in gastro-intestinal fluid and belongs to BCS (Biopharmaceutical Classification System) class II drugs.[39,40] By the selection of specific excipients; scientists not only enhanced the solubility and bioavailability, but also modify the target site and protection from first pass effect.[41] It is also evaluated that different approaches can be used for increasing gastrointestinal residence time by magnetic system, high

Table I: Microencapsulation techniques and outcomes

Type of microencapsulation	Study years	First author name	Study design	Outcomes	Quality of Evidence [35]
Hot-melt extrusion method	2024	Nnamdi Ikemefuna Okafor	Clinical study	Improve the palatability and taste masking of pediatric oral formulations.[36]	Moderate
Solvent evaporation method	2014	Rejendar R. Mallepally	Experimental study	Microencapsulation of miscible and immiscible phases.[37]	High
Fluid bed coating/ Air suspension coating	2017; 2019	J. Mandic; Mohammad Foroughi-Dahr; Samar Elasmaligy	Experimental studies	Taste masking and linear release for modified release products.[38, 39]	High; Moderate
Phase separation / Coacervation method	2022	Ruifeng Wang	Experimental study	Paddle stirring can be customized to produce desired particle size of encapsulated material.[20]	Moderate
Spray drying	2020	Jiayue Guo	Experimental study	Manufacturing of finer, spherical and regular particle.[21]	Low
Hot melt	2015	Manjeet B. Pimparade	In-vitro, In-vivo experimental study	Effective taste masking, and maintaining structure crystallinity of API (Active Pharmaceutical Ingredient).[40]	High

density system, muco-adhesive system, swelling and expanding system as well as floating system.[42] Floating system can easily have achieved by applying multi-layer coating as a source of CO_2 along with extended time for drug release.[42] Processing parameters like, inlet air, inlet temperature, fluidization, spray rate, spray speed, dispersion contents and viscosity plays the vital role to achieve product yield, content uniformity and product performance.[42] Drug protection from the low pH and enzyme of stomach is also a challenge for formulators.[42] Application of specific excipients by microencapsulation drug substances have been protected from degradation by GIT environmental factors and enhances the product stability.[43] Repeated dosage intake is a challenge to manage patient compliance and adherence to treatment course. To avoid that noncompliance high potency with extended release period is required. Microencapsulation with fluid bed coating technique has resolved this issue. To achieve that goal; different formulation using various polymers have been designed. Currently one of these formulations is discussed in this review included diclofenac sodium sustain release pellets.[38,43]

Pediatric dosage acceptance is also a challenge; many drugs with bitter taste are used for treatment. Due to bitter taste, it is not possible to give medication in as such form to children. Different dosage forms like tablets and capsules are also not acceptable by children. Fluid bed coating by microencapsulation technique for taste masking of bitter drugs like clarithromycin have been achieved.[43] Similarly, safe delivery of probiotic to support antibiotic for treatment of bacterial infection is another challenge for formulator. One of the problem associated with their transfer to site of action is the gastric path and their time dependent release. These problem have been resolved by spray drying technique. After spray drying, probiotic is converted into erodible tablets using beeswax and carboxymethylcellulose sodium.[44] These excipients not only delayed the probiotic release but also prevent from acidic environment of gastrointestinal tract, ensure intestinal colonization and vaginal mucosa for support of effective treatment.[44]

Retinol is an important retinoid for the treatment of acne, wrinkle, aging induced by UV (Ultraviolet) light and for treatment of chronic skin condition like psoriasis and ichthyosis.[45] That compound is degraded when exposed to light and oxygen; in as such form it is very difficult to incorporate in dosage form. So, to protect this compound from environmental factors to enhance its stability; microencapsulation technique was applied; the technique not only improve its stability but also reduced

Table II: Clinical and pharmaceutical benefits of microencapsulation techniques

Microencapsulated Product	Study years	First author name	Study design	Outcomes	Quality of Evidence [35]
Lactobacillus and *Bifidobacterium* as probiotics	2024	M. Lavanya	Experimental animal study	Polymeric or lipid-based nanoparticles improved the bioavailability of probiotics and inhibited the neuro-degeneration which caused by Alzheimer's disease.[41]	High
Ibuprofen	2013	N. Carreras	Experimental study (Solvent evaporation method)	Taste masking.[42]	Moderate
Adipose tissue	2018	Seongjae Choi	Animal study	Treatment of osteoarthritis.[43]	Moderate
Fenretinide	2020	Kari Nieto	In-vitro, In-vivo experimental study	Drug solubility enhancement.[26]	High
Bifidobacterium breve BC204	2018	Barbara Giordani	In-vitro, Ex-vivo experimental study	Protection from gastrointestinal and urogenital infections.[44]	Low
Moringa olifera leaf extract	2023	Jaine Mailho Gimenis	In-vitro, In-vivo experimental study	Product stability.[27]	Low
Thymoquinone	2020	Hamzeh Alkhatib	Full factorial (3^2) design study	Taste masking.[45]	High
Diclofenac sodium	2022	Nesrin F. Taha	In-vitro, In-vivo experimental study	Reduction in side effects.[46]	High
$Reti_{nol}$	2018	C. Wyatt Shields IV	Double blind human study	Product safety and reduction of toxic effects.[47]	Moderate
Omeprazol	2019	Federica Ronchi	Experimental study	Oral route stability of API (Active Pharmaceutical Ingredient).[30]	Moderate
Clarithromycin	2012	Harshada Sanjay Akre	Experimental study	Taste masking.[48]	High

the toxic effect e.g. skin irritation. The suitable excipient for microencapsulation is selected i.e. silicone due to biocompatibility and stability. The encapsulation of retinol is done by using phase separation technique.[45]

The most common form of arthritis is the osteoarthritis, which is degenerative disease of joints.[45] It commonly affects quality of life by causing pain, stiffness and disability. Various types of techniques have been applied for the treatment of this condition for the regeneration of joints. Among different techniques, adipose tissue derived mesenchymal stem cell have better control over other methods.[46] The technique improved quality of life in human after intra-articular injection of adipose tissue mesenchymal stem cells by reducing pain, knee joint cartilage defects and improving functionality.[47] These adipose tissue mesenchymal stem cells are alginate base microencapsulated.[47] These microencapsulated adipose tissue mesenchymal cells act as mechanical barrier, extracellular material and improves cell viability; which also allow release of stem cell produced growth factors and substances that act as anti-inflammatory for surrounding effected area.[48]

The plant oriented herb from Moringa oleifera L. has many health benefits. It is an important antioxidant and provide protection against various conditions by having characteristics of hypoglycemia, antimicrobial, anti-inflammatory, antispasmodic, antiasthmatic and hypocholesterolemic.[49] Skin is the largest organ of the body and provides protection against foreign invaders. Due to antioxidant activity of moringa leaf extract it provides protection to skin from stress oxidation, which leads to wrinkles and aging.[49] To obtain maximum

pharmacological effect for body, it is very important to obtain stable formulation. For this purpose, it is now possible to obtain moringa leaf extract liposomes by microencapsulation technique.[49]

CONCLUSION

Drug development by microencapsulation technique is having wide ranging beneficial clinical implications. Microencapsulated products have superiority compared to other product in reference to their uniformity, bioavailability, toxicity, stability and patient acceptance.

Limitations and recommendations:

There are many issues related to the advancement of microencapsulation techniques. Despite advancements, selection of core material, material required for coating e.g. cheaper biopolymer and processing are still challenges for pharmaceutical scientists. More studies on bioassays are required for encapsulation of food anti-oxidants. Due to high cost of manufacturing of microencapsulated products; few pharmaceutical industries are having interest in this technique. In Pakistan, the only techniques applied for microencapsulation is fluid bed coating. Organ specific drug delivery is another challenge for this product. The advancement in this area is possible with research institute and technology transfer, which should be supported at national level.

Authors' contributions:

Sheikh Abdul Khaliq: Critical Review, Facilitated for Reagents / Material Analysis

Sarfraz Ahmad: Experimentation/ Study Conduction, Manuscript Writing

Kamran Haidar: Conception of study/ Designing/ Planning, Experimentation / Study Conduction

Muhammad Jiyad Shaikh: Experimentation/ Study Conduction, Analysis/ Interpretation/ Discussion

REFERENCES

1. Aghazadeh H, Tamaddon F, Ouni M, Taheri P, Sangchooli T. Microencapsulation of herbal bioactive drug by Chlorella Vulgaris microalgae as a nano-formulation for drug delivery to cells. J Eurasian Chem Commun. 2023;5(4):327-34. https://doi.org/10.22034/ecc.2023.370804.1558
2. Ricardo F, Pradilla D, Luiz R, Alvarez Solano OA. A multi-scale approach to microencapsulation by interfacial polymerization. Polymers. 2021;13(4):01-13. https://doi.org/10.3390/polym13040644.
3. Bassand C, Freitag J, Benabed L, Verin J, Siepmann F, Siepmann J. PLGA implants for controlled drug release: Impact of the diameter. Eur J Pharm Biopharm. 2022;177(1):50-60. https://doi.org/10.1016/j.ejpb.2022.05.020.
4. Pei Y, Wang J, Khaliq NU, Meng F, Oucherif KA, Xue J, et al. Development of poly (lactide-co-glycolide) microparticles for sustained delivery of meloxicam. J Control Release. 2023;353:823-31. https://doi.org/10.1016/j.jconrel.2022.12.019.
5. Luo S, Gao M, Pan X, Wang Y, He Y, Zhu L, et al. Fragrance oil microcapsules with low content of formaldehyde: Preparation and characterization. Colloids and Surfaces: Physicochemical and Engineering Aspects. 2022;648(1):01-23. https://doi.org/10.1016/j.colsurfa.2022.129019.
6. Raj GB, Dash KK. Microencapsulation of betacyanin from dragon fruit peel by complex coacervation: Physicochemical characteristics, thermal stability, and release profile of microcapsules. J Food Bioscience. 2022;49(1):01-10. httpd;//doi.org/10.1016/j.fbio.2022.101882.
7. Ghiorghita CA, Dinu MV, Dragan ES. Burst-free and sustained release of diclofenac sodium from mesoporous silica/PEI microspheres coated with carboxymethyl cellulose/chitosan layer-by-layer films. Cellulose. 2022;29(1):395-412. https://doi.org/10.1007/s10570-021-04282-y.
8. Marikar SN, El-Osta A, Johnston A, Such G, Al-Hasani K. Microencapsulation-based cell therapies. Cellular and Molecular Life Sciences. 2022;79(7):01-13. https://doi.org/10.1007/s00018-022-04369-0.
9. Osmałek T, Froelich A, Jadach B, Tatarek A, Gadziński P, Falana A, et al. Recent advances in polymer-based vaginal drug delivery systems. Pharmaceutics. 2021;13(6):01-49. https://doi.org/10.3390 /pharmaceutics13060884.
10. Mewada V, Shah J, Jacob S, Shah H, Boddu SH, Nair AB. Improvement of Bioavailability of Sildenafil Citrate

Through Taste Masked Orodispersible Film for Pulmonary Hypertension Management. AAPS PharmSciTech. 2024;25(7):01-39. https://doi.org/10.1208/s12249-024-02905-8.

11. Sutthapitaksakul L, Thanawuth K, Dass CR, Sriamornsak P. Optimized taste-masked microparticles for orally disintegrating tablets as a promising dosage form for Alzheimer's disease patients. Pharmaceutics. 2021;13(7):01-22. https://doi.org/10.3390/pharmaceutics13071046.
12. Dung PT, Trinh TD, Nguyen QH, Nguyen HM, Nguyen NC, Tran NB, et al. Development of taste-masking microcapsules containing azithromycin by fluid bed coating for powder for suspension and in vivo evaluation. Journal of Microencapsulation. 2023;40(5):345-56. https://doi.org/10.1080/02652048.2023.2209639.
13. Xu J, Lin Y, Zawaneh PN, Nestorov I, Leung CY, Boulas P. Prediction of in vivo performance of oral extended release formulations prior to clinical evaluation: A case study for enteric coated polymeric beads formulation. Eur J Pharm Biopharm. 2021;158(1):222-32. https://doi.org/10.1016/j.ejpb.2020.11.023.
14. Mohanty D, Zafar A, Jafar M, Upadhyay AK, Haque MA, Gupta JK, et al. Development, in-vitro characterization and preclinical evaluation of esomeprazole-encapsulated proniosomal formulation for the enhancement of anti-ulcer activity. Molecules. 2022;27(9):01-17. https://doi.org/10.3390/molecules27092748.
15. Luo S, He Y, Zhu L, Si T, Sun Y. Comprehensive evaluation on the encapsulation performances of melamine-formaldehyde microcapsules affected by core oils. Colloids and Surfaces A: Physicochemical and Engineering Aspects. 2023;659(1):01-44. https://doi.org/10.1016/j.colsurfa.2022.130794.
16. Zhao H, Fei X, Liang C, Xian Z, Cao L, Yang T. The evaluation and selection of core materials for microencapsulation: A case study with fragrances. Flavour and Fragrance Journal. 2021;36(6):652-61. https://doi.org/10.1002/ffj.3675.
17. Ahangaran F. Microencapsulation: Solvent evaporation. In: Sefat F, Farzi G, Mozafari M, editors. Principles of Biomaterials Encapsulation: Volume One.1st ed. Bradford, United Kingdom: Elsevier; 2023. p. 377-92. https://doi.org/10.1016/B978-0-323-85947-9.00016-9.
18. Frey C. Fluid bed coating-based microencapsulation. In: Sobel R, editor. Microencapsulation in the food industry. 1. 2nd ed. Illinois, USA: Elsevier; 2023. p. 83-115. https://doi.org/10.1016/B978-0-12-821683-5.00024-8.
19. Farzi G, Gheysipour M. Microencapsulation: Air suspension technique. In: Sefat F, Farzi G, Mozafari M, editors. Principles of Biomaterials Encapsulation: Volume One. 1st ed. Bradford, United Kingdom: Elsevier; 2023. p. 297-303. https://doi.org/10.1016/B978-0-323-85947-9.00021-2.
20. Wang R, Bao Q, Clark AG, Wang Y, Zhang S, Burgess DJ. Characterization and in vitro release of minocycline hydrochloride microspheres prepared via coacervation. Int J Pharm. 2022;628(2): https://doi.org/10-24. 10.1016/j.ijpharm.2022.122292.
21. Guo J, Li P, Kong L, Xu B. Microencapsulation of curcumin by spray drying and freeze drying. LWT- Food Science and Technology. 2020;132(1):92-8. https://doi.org/10.1016/j.lwt.2020.109892.
22. Liu T, Wang J, Feng Y, Wang H, Xu Y, Yin T, et al. Further enhancement of the sustained-release properties and stability of direct compression gel matrix bilayer tablets by controlling the particle size of HPMC and drug microencapsulation. Powder Technology. 2024;448(1):01-45. https://doi.org/10.1016/j.powtec.2024.120256.
23. Lubis LD, Prananda AT, Juwita NA, Nasution MA, Syahputra RA, Sumaiyah S, et al. Unveiling antioxidant capacity of standardized chitosan-tripolyphosphate microcapsules containing polyphenol-rich extract of Portulaca oleraceae. Heliyon. 2024;10(8):01-13. https://doi.org/10.1016/j.heliyon.2024.e29541
24. Ponjavić M, Nikolić MS, Jevtić S, Jeremić S, Đokić L, Đonlagić J. Star-shaped poly (ε-caprolactones) with well-defined architecture as potential drug carriers. Journal of the Serbian Chemical Society. 2022;87(9):1075-90. https://doi.org/10.2298/JSC220202032P.
25. Abbas SEM, Maged G, Wang H, Lotfy A. Mesenchymal Stem/Stromal Cells Microencapsulation for Cell Therapy. Cells. 2025;14(3):01-24. https://doi.org/10.3390/cells14030149.

26. Nieto K, Mallery SR, Schwendeman SP. Microencapsulation of Amorphous Solid Dispersions of Fenretinide Enhances Drug Solubility and Release from PLGA in vitro and in vivo. International journal of pharmaceutics. 2020;586(1):01-12. https://doi.org/10.1016/j.ijpharm.2020.119475.
27. Gimenis JM, Figueiredo CCM, da Costa Gomes A, Granero FO, Ximenes VF, Silva LP, et al. Microencapsulation of Moringa oleifera L. extract in liposomes: Evaluation of antioxidant and antiglycation activities, cytotoxicity and skin biometric parameters. Journal of Drug Delivery Science Technology. 2023;88(1):01-14. https://doi.org/10.1016/j.jddst.2023.104972.
28. Alkhatib H, Mohamed F, Akkawi ME, Alfatama M, Chatterjee B. Microencapsulation of black seed oil in alginate beads for stability and taste masking. Journal of Drug Delivery Science. 2020;60(1):1-13. https://doi.org/10.1016/j.jddst.2020.102030.
29. Taha NF, Dyab AK, Emara LH, Meligi NM. Microencapsulation of Diclofenac Sodium into natural Lycopodium clavatum spores: In vitro release and gastro-ulcerogenic evaluations. J Drug Deliv Sci. 2022;71(1):1-12. https://doi.org/10.1016/j.jddst.2022.103278.
30. Ronchi F, Sereno A, Paide M, Sacré P, Guillaume G, Stéphenne V, et al. Development and evaluation of an omeprazole-based delayed-release liquid oral dosage form. Int J Pharm. 2019;567(1):1-18. https://doi.org/10.1016/j.ijpharm.2019.06.007.
31. Parente JF, Sousa VI, Marques JF, Forte MA, Tavares CJ. Biodegradable polymers for microencapsulation systems. Advances in polymer technology. 2022;2022(1):01-43. https://doi.org/10.1155/2022/4640379.
32. Lopez-Mendez TB, Santos-Vizcaino E, Pedraz JL, Hernandez RM, Orive G. Cell microencapsulation technologies for sustained drug delivery: Clinical trials and companies. Drug Discov Today. 2021;26(3):852-61. https://doi.org/10.1016/j.drudis.2020.11.019.
33. Bhalala K, Jadeja D, Dudhat K. Microspheres: Preparation Methods, Advances, Applications, and Challenges in Drug Delivery. Biomedical Materials & Devices. 2025;1(1):1-40. https://doi.org/10.1007/s44174-025-00281-w.
34. Lindsey WT, Olin BR, Hansen RA. Systematic Review and Meta-Analysis, Chapter 14. 2nd ed. Aparasu RR, Bentley JP, editors. USA: McGraw-Hill Education; 2020. p 151-160. https://doi.org/10.1111.98074578/PRS.
35. Alonso-Coello P, Schünemann HJ, Moberg J, Brignardello-Petersen R, Akl EA, Davoli M, et al. GRADE Evidence to Decision (EtD) frameworks: a systematic and transparent approach to making well informed healthcare choices. BMJ. 2016;353(1):01-10. https://doi.org10.1136/bmj.i2016.
36. Okafor NI. Microencapsulation Techniques in HIV Pediatric Formulations: Advances and Future Outlook. Advances in Pharmacological and Pharmaceutical Sciences. 2024;2024(1):01-21. https://doi.org/10.1155/2024/5081655.
37. Mallepally RR, Parrish CC, Mc Hugh MA, Ward KR. Hydrogen peroxide filled poly (methyl methacrylate) microcapsules: potential oxygen delivery materials. Int J Pharm Sci. 2014;475(1-2):130-7. https:doi.org/10.1016/j.ijpharm.2014.08.052.
38. Mandić J, Luštrik M, Vrečer F, Gašperlin M, Pobirk AZ. Solidification of carvedilol loaded SMEDDS by swirling fluidized bed pellet coating. Int J Pharm. 2019;566(1-2):89-100. https://doi.org/10.1016/j.ijpharm.2019.05.055.
39. Foroughi-Dahr M, Mostoufi N, Gharebagh RS, Chaouki J. Particle coating in fluidized beds. Int J Pharm. 2017;20(1):171-86. https://doi.org/10.1016/j.ijpharm.2019.02.023.
40. Pimparade MB, Morott JT, Park JB, Kulkarni VI, Majumdar S, Murthy S, et al. Development of taste masked caffeine citrate formulations utilizing hot melt extrusion technology and in vitro–in vivo evaluations. Int J Pharm. 2015;487(1-2):167-76. https://doi.org/10.1016/j.ijpharm.2015.04.030.
41. Lavanya M, Namasivayam SKR, Priyanka S, Abiraamavalli T. Microencapsulation and nanoencapsulation of bacterial probiotics: new frontiers in Alzheimer's disease treatment. Biotech. 2024;14(12):01-33. https://doi.org/10.1007/s13205-024-04158-5.

42. Carreras N, Acuña V, Martí M, Lis M. Drug release system of ibuprofen in PCL-microspheres. J Colloid Polymer Science. 2013;291(1):157-65. https://doi.org/10.1007/s00396-012-2768-x.

43. Choi S, Kim J-H, Ha J, Jeong B-I, Jung YC, Lee G-S, et al. Intra-articular injection of alginate-microencapsulated adipose tissue-derived mesenchymal stem cells for the treatment of osteoarthritis in rabbits. J Stem cells international. 2018;2018(1):1-11. https://doi.org/10.1155/2018/2791632.

44. Giordani B, Melgoza LM, Parolin C, Foschi C, Marangoni A, Abruzzo A, et al. Vaginal Bifidobacterium breve for preventing urogenital infections: Development of delayed release mucoadhesive oral tablets. Int J Pharm. 2018;550(1-2):455-62. https://doi.org/10.1016/j.ijpharm.2018.09.003.

45. Alkhatib H, Mohamed F, Akkawi ME, Alfatama M, Chatterjee B. Microencapsulation of black seed oil in alginate beads for stability and taste masking. J Drug Deliv Sci Technol. 2020;60(1):01-13. https://doi.org/10.1016/j.jddst.2020.102030.

46. Shields IV CW, White JP, Osta EG, Patel J, Rajkumar S, Kirby N, et al. Encapsulation and controlled release of retinol from silicone particles for topical delivery. J Control Release. 2018;278(1):37-48. https://doi.org/10.1016/j.jconrel.2018.03.023.

47. Akre HS, Mundhada DR, Bhaskaran S, Asghar S, Gandhi GS. Dry suspension formulation of taste masked antibiotic drug for pediatric use. Journal of Applied Pharmaceutical Science. 2012;2(7):166-71. https://doi.org/10.7324/JAPS.2012.2725.

48. Elsamaligy S, Bodmeier R. Development of extended release multiple unit effervescent floating drug delivery systems for drugs with different solubilities. J Drug Deliv Sci Technol. 2015;30(B1):467-77. https://doi.org/10.1016/j.jddst.2015.05.008.

49. Pareek A, Pant M, Gupta MM, Kashania P, Ratan Y, Jain V et al. Moringa oleifera: An Updated Comprehensive Review of Its Pharmacological Activities, Ethnomedicinal, Phytopharmaceutical Formulation, Clinical, Phytochemical, and Toxicological Aspects. Int J Mol Sci. 2023 Jan 20;24(3):2098. https://doi.org/10.3390/ijms24032098

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