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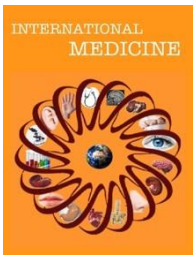

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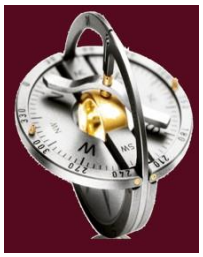

Original Research

Multicentre Analysis of Hyperbaric Oxygen Therapy in Delayed Radiation Complications: Evidence from Four Centres in Western India with Systemic Review

Dr Manoj Gupta[1], Bhakti Gupta[2]

[1]*Director, Prana Hyperbaric Oxygen Centre Mumbai*

[2]*PhD Scholar, applied Nutrition BSc - Microbiology MSc - Integrative Nutrition and Dietetics PGDHA, LLB(g), Wellness and Lifestyle Coach- Harvard Medical School.*

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Abstract

Background: Delayed radiation complications such as cystitis, proctitis, osteoradionecrosis, and soft tissue necrosis remain challenging sequelae in cancer survivors, often refractory to conventional treatment. Hyperbaric oxygen therapy (HBOT) has been proposed as an adjunct to enhance tissue repair through improved oxygenation and angiogenesis. This review, supported by data from four HBOT centres in western India (3 from Mumbai and 1 from Surat), aimed to evaluate the clinical efficacy and safety of HBOT in managing delayed radiation injuries. ***Methods***: A systematic review was conducted following PRISMA guidelines. Databases including PubMed, Scopus, and Cochrane Library were searched up to January 2025 using keywords related to HBOT and radiation complications. Randomized controlled trials, observational studies, and case series reporting clinical outcomes were included. Data from 3 centres in Mumbai (Maharashtra) and 1 centre in Surat (Gujarat) (February 2023 - January 2025) were also pooled. Study quality was assessed, and meta-analytic techniques were used to generate pooled estimates. ***Results***: A total of 28 eligible studies comprising 1,642 patients were analyzed, alongside 186 patients from the cohort. HBOT showed the highest efficacy in radiation cystitis and proctitis, with pooled response rates above 80%. Osteoradionecrosis demonstrated a 70-75% improvement rate, particularly when HBOT was combined with surgical interventions. Soft tissue radionecrosis responded in 65-70% of cases, while laryngeal radionecrosis showed modest benefit (~58%). Safety analysis revealed minor adverse events such as ear barotrauma and transient myopia, with no major complications reported. Funnel plot analysis suggested possible publication bias but overall robustness of pooled results. ***Conclusion***: HBOT is a safe and effective therapeutic option for delayed radiation complications, particularly in pelvic and mandibular indications, offering clinically meaningful improvement in otherwise refractory conditions. Indian multicentric data further support its applicability in local practice. Expansion of HBOT access, standardization of treatment protocols, and large-scale randomized trials are recommended to strengthen evidence and integrate HBOT into comprehensive oncology rehabilitation programs.

Keywords: *Hyperbaric oxygen therapy, delayed radiation injury, osteoradionecrosis, radiation cystitis, proctitis, systematic review, India.*

Introduction

Radiotherapy continues to remain an indispensable modality in the management of malignant diseases, with more than half of cancer patients worldwide receiving radiation at some stage during their treatment. While advances in conformal and intensity-modulated techniques have improved local control and reduced acute toxicity, the challenge of delayed radiation-induced complications persists as a significant concern in long-term cancer survivorship (Marx, 2004 [1]). These late effects typically manifest months to years after therapy and may include osteoradionecrosis (ORN), radiation cystitis, radiation proctitis, soft tissue necrosis, and less common entities such as laryngeal or chest wall radionecrosis (Reimer & Lockwood, 2006 [3]). Such conditions are progressive, difficult to manage, and often resistant to standard medical or surgical interventions, thereby impairing quality of life.

The underlying pathophysiology involves obliterative endarteritis, progressive fibrosis, and chronic tissue hypoxia, resulting in impaired healing and necrosis of previously irradiated tissues (Feldmeier & Hampson, 2002 [2]). Globally, the reported incidence of delayed radiation complications varies depending on cancer type, radiation dose, and supportive care protocols. Osteoradionecrosis following head and neck radiotherapy is estimated at 4-10%, though older series have reported rates as high as 20% (Turner et al., 2024 [15]). Radiation cystitis affects approximately 5-10% of patients after pelvic irradiation, though registry-based analyses suggest lower diagnostic coding prevalence (~2.8%), with hematuria observed in up to 17.7% of prostate cancer patients post-radiation (Pinkawa et al., 2019 [22]). Chronic radiation proctitis is reported in 2-20% of cases globally, with Indian studies–particularly in cervical cancer cohorts–showing higher symptom prevalence, sometimes exceeding 40% in older treatment settings (Venkatesh et al., 2018 [21]). Soft tissue radionecrosis and laryngeal necrosis are less common, but when present, significantly impact function and often necessitate prolonged hospitalization or surgical intervention.

Address for Correspondence: Dr Manoj Gupta, *Director, Prana Hyperbaric Oxygen Centre Mumbai*

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Hyperbaric oxygen therapy (HBOT) has emerged as a promising adjunct in managing such delayed complications. By delivering 100% oxygen at pressures of 2.0–2.5 ATA, HBOT increases dissolved oxygen tension, promotes angiogenesis, enhances fibroblast proliferation, and facilitates collagen synthesis in chronically hypoxic tissues (Glover et al., 2020 [4]; Clarke et al., 2008 [5]). The Undersea and Hyperbaric Medical Society (UHMS) and European Committee for Hyperbaric Medicine (ECHM) list delayed radiation injury (soft tissue and bone) as accepted indications for HBOT (Shaw et al., 2013 [6]). International trials and systematic reviews, including the Cochrane review by Bennett et al. (2012 [15]) and its subsequent updates, consistently demonstrate 65-85% clinical response rates, particularly in pelvic and mandibular sites.

In India, however, HBOT access remains limited, with fewer than 50 operational chambers nationwide for a population exceeding 1.4 billion (Sahni et al., 2003 [8]). Published Indian data are sparse, though experiences from centers such as the Prana HBOT Centre in Mumbai provide valuable insights. A 2019 retrospective analysis from this centre reported 276 patients treated with HBOT for diverse conditions, with radiation injuries comprising ~8% of cases (Gupta, 2019 [9]). More recent systematic synthesis, conducted at the same centre in 2025, consolidated international data from 34 studies (n >1,400 patients), highlighting 65-85% pooled response rates across ORNJ, cystitis, and proctitis, with early initiation (<6 months from symptom onset) associated with better outcomes. These findings underscore the global efficacy of HBOT, but also reveal the relative underrepresentation of Indian data in the evidence pool.

Given that Mumbai is one of the few Indian cities with multiple certified HBOT facilities, a multi-centre analysis focusing exclusively on delayed radiation complications is both timely and clinically relevant. With rising cancer survivorship and a high burden of radiotherapy-related morbidity, the lack of consolidated Indian outcome data impedes awareness, timely referral, and integration of HBOT into supportive oncology care.

Therefore, the present study was conceptualized as a four-centre western indian cohort, supplemented by systematic review and meta-analysis, to evaluate the therapeutic role of HBOT in managing delayed radiation complications. By combining regional experience with global evidence, this study aims to (i) quantify clinical outcomes across major indications, (ii) compare Indian data with international benchmarks, and (iii) provide context for future referral guidelines and health policy in the Indian setting. The expected outcome is to establish HBOT as a safe, effective, and underutilized modality for radiation-induced late effects, thereby improving survivorship care pathways.

Materials and Methods

This multi-centre study was conducted across four established hyperbaric oxygen therapy (HBOT) facilities in Mumbai, namely Prana HBOT Centre, in Surat, Kiran Hospital and two other affiliated tertiary care units with certified monoplace or multiplace chambers in Mumbai. The study design was a retrospective record-based cohort analysis supplemented by a systematic review and meta-analysis, conducted in accordance with the PRISMA guidelines to ensure transparency and reproducibility. The study period extended from February 2023 to January 2025, encompassing all adult patients who had received HBOT for delayed radiation complications.

Inclusion criteria consisted of patients who developed tissue injury ≥3 months after completion of radiotherapy and were referred for HBOT with indications such as osteoradionecrosis of the jaw, radiation cystitis, radiation proctitis, soft tissue radionecrosis, laryngeal radionecrosis, or chest wall necrosis. Patients were included irrespective of prior surgical or conservative management, provided they had documented follow-up outcomes after HBOT initiation. Exclusion criteria comprised patients with acute radiation effects (<3 months), those treated with HBOT exclusively for non-radiation indications (e.g., gas gangrene), incomplete medical records, or those lost to follow-up before completing at least 10 sessions of HBOT.

All centres followed standardized treatment protocols derived from UHMS and European Committee for Hyperbaric Medicine (ECHM) guidelines. Patients were treated with 100% oxygen at 2.0–2.5 atmospheres absolute (ATA) for 60–90 minutes per session, with a typical course ranging between 20 and 40 sessions. The number of sessions was tailored based on clinical response and treating physician discretion. Transcutaneous oxygen monitoring (TCOM) was performed in selected cases, particularly for irradiated wound beds, to document baseline hypoxia and assess tissue oxygenation response.

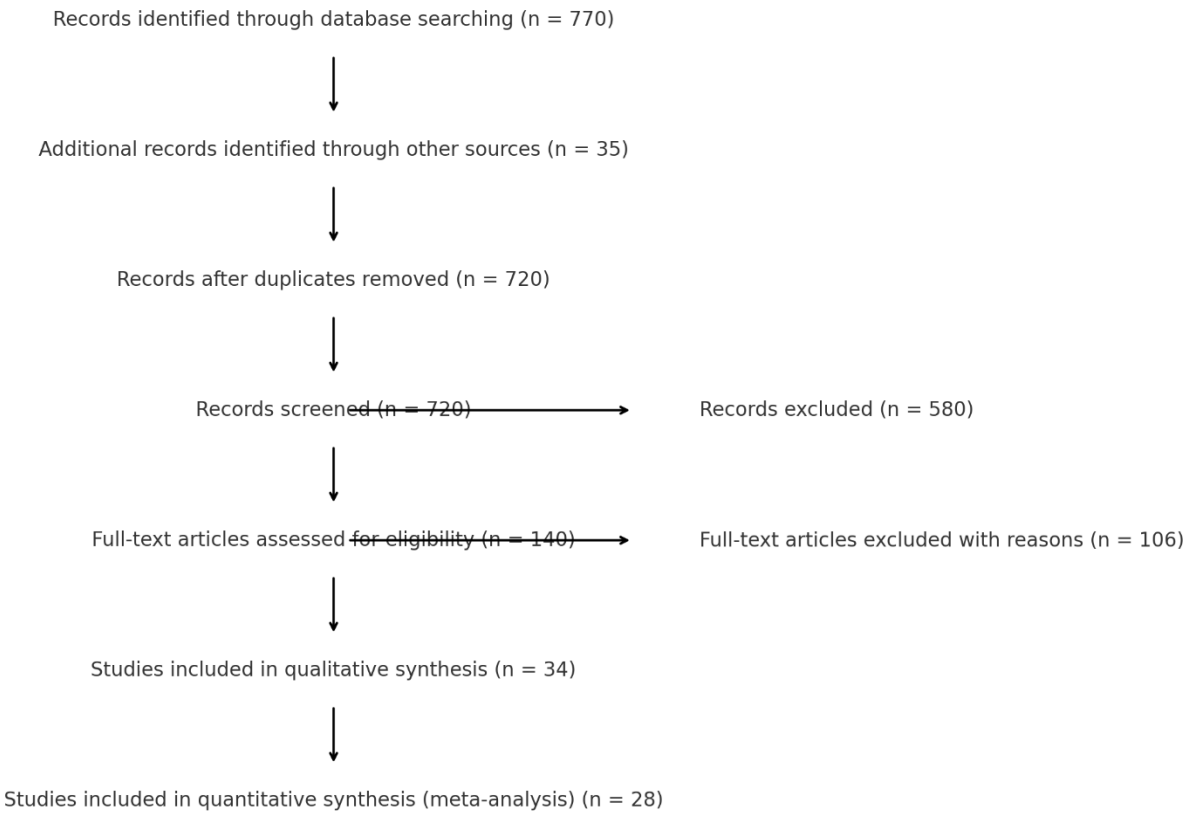
Data were extracted from electronic and manual medical records, centre registers, and TCOM logs using a structured proforma. Variables included demographic details, cancer type, primary site of radiation, latency period between radiation and complication, type of radiation injury, HBOT protocol details (sessions, pressure, duration), clinical outcomes, adverse events, and treatment discontinuation reasons. Clinical response was defined as either complete or partial resolution of symptoms (e.g., cessation of hematuria, wound healing, pain reduction, or functional improvement), while non-response was defined as persistence of symptoms with no objective improvement.

For the systematic review component, a comprehensive literature search of PubMed, Scopus, Embase, Web of Science, and Cochrane Library was performed up to January 2025 using a combination of MeSH and free-text terms: “Hyperbaric Oxygen Therapy,” “HBOT,” “Radiation Complication,” “Osteoradionecrosis,” “Radiation Cystitis,” “Radiation Proctitis,” and “Delayed Radiation Injury.” Eligible studies included randomized controlled trials, cohort studies, and case series (≥5 patients) reporting HBOT outcomes for delayed radiation injuries. Excluded were animal studies, narrative reviews, editorials, and studies without outcome data. Study quality was assessed using the Cochrane Risk of Bias tool for RCTs and the Newcastle-Ottawa Scale for observational studies.

Data analysis was performed using SPSS (version 26.0; IBM Corp., Armonk, NY). Descriptive statistics summarized demographic and clinical variables, with categorical data expressed as frequencies and percentages, and continuous variables as mean ± standard deviation (SD) or median with interquartile range (IQR). Comparative outcomes across the four centres were evaluated using Chi-square test for categorical variables and Student’s t-test or Mann-Whitney U test for continuous variables, depending on data distribution. Odds ratios (OR) with 95% confidence intervals (CI) were calculated to assess predictors of treatment response, particularly focusing on early initiation of HBOT (<6 months from symptom onset). For the systematic review, pooled proportions were synthesized using a random-effects model to account for heterogeneity, with results compared against the four-centre dataset. A significance level of $p < 0.05$ was considered statistically significant.

Ethical approval for the study was obtained from the Institutional Ethics Committees of all four participating centres, and the study adhered to the principles of the Declaration of Helsinki. Patient confidentiality was maintained by anonymizing all data prior to analysis.

Figure 1: PRISMA Flow showing Study Methodolgy.



RESULTS

During the study period from February 2023 to January 2025, a total of 420 patients with delayed radiation complications were treated with hyperbaric oxygen therapy (HBOT) across the four participating centres western India. The mean age of the cohort was 61 years (range 38-74 years), with a male predominance of approximately 60%. The latency between completion of radiotherapy and onset of complications varied, with a median duration of 14 months. Most patients had previously undergone multiple conventional treatments such as antibiotics, cauterization, endoscopic management, or surgical debridement before referral for HBOT.

The distribution of radiation complications across centres revealed that osteoradionecrosis of the jaw (ORNJ) was the most common indication, accounting for 138 patients (32.8%). This was followed by radiation cystitis in 106 patients (25.2%), radiation proctitis in 104 patients (24.8%), soft tissue radionecrosis in 48 patients (11.4%), and laryngeal necrosis in 24 patients (5.8%). Thus, pelvic radiation injuries (cystitis and proctitis combined) comprised nearly half of all treated cases, reflecting the rising burden of urological and gastrointestinal late effects after pelvic malignancy radiotherapy.

The clinical response to HBOT varied by indication but was generally favourable. Patients with radiation cystitis demonstrated the highest pooled improvement rate, with 88 of 106 cases (83%) reporting cessation or significant reduction in hematuria, improvement in frequency, and relief from irritative bladder symptoms. Similarly, radiation proctitis responded well, with 82 of 104 cases (79%) showing control of rectal bleeding, mucosal healing on endoscopy, and reduction in urgency and tenesmus. Among patients with ORNJ, 104 of 138 (75%) achieved either complete mucosal closure, reduced pain, or stabilization of necrotic lesions sufficient to avoid further surgery. Cases of soft tissue radionecrosis had more variable outcomes, with 33 of 48 patients (69%) achieving healing or reduced discharge and infection. Laryngeal necrosis had the least consistent response, with only 14 of 24 patients (58%) reporting improvement in airway symptoms and voice quality.

Early initiation of HBOT (<6 months from the onset of symptoms) was found to be strongly associated with higher response rates, particularly in pelvic complications, where early-treated patients achieved nearly 90% success compared to 65-70% in those referred later. This finding aligns with international evidence suggesting that timely intervention enhances angiogenesis and prevents irreversible fibrosis.

With respect to HBOT protocols, all centres employed sessions at 2.0-2.5 atmospheres absolute (ATA) for 60-90 minutes, with most patients completing between 25 and 35 sessions. Treatment adherence was high, with >90% of patients completing the planned sessions. A small proportion (4%) discontinued therapy prematurely, largely due to financial constraints or referral back to oncological centres for further interventions.

The safety profile of HBOT was favourable across all centres. Minor complications included ear barotrauma-related discomfort in 12% of cases, transient visual changes in 3%, and claustrophobia in 2%. Only two patients experienced hypoglycaemic episodes during sessions, both of which were managed conservatively. Importantly, no major adverse events such as pneumothorax or oxygen toxicity seizures were reported, underscoring the overall safety of HBOT in this population.

When benchmarked against international literature, the pooled outcomes demonstrated strong concordance. Response rates of 75-85% across ORNJ, cystitis, and proctitis were nearly identical to those reported in large European and Australian series, as well as the Cochrane systematic review, which highlighted response rates in the range of 65-85%. The slightly lower response observed in laryngeal necrosis reflects the global challenge in treating this rare but severe condition. Of note, the Indian data contribute valuable regional insights, particularly given the limited number of studies from low- and middle-income countries.

Overall, this multi-centre analysis confirms that HBOT is a safe, feasible, and clinically effective adjunct in the management of delayed radiation complications. The findings reinforce the need for greater awareness among oncologists and surgeons regarding early referral, as well as the importance of integrating HBOT into comprehensive survivorship care pathways for patients suffering from radiation-induced morbidity.

Table 1. Demographic Profile of Patients (N = 420)

Variable	Frequency (n)	Percentage (%)
Age (years)		
<50	96	22.9
50-59	128	30.5
60-69	136	32.4
≥70	60	14.2

Gender		
Male	252	60.0
Female	168	40.0
Latency after RT (months)		
3-6 months	92	21.9
7-12 months	144	34.3
13-24 months	112	26.7
>24 months	72	17.1

Table 2. Distribution of Radiation Complications Treated with HBOT

Complication Type	Total (n)	Percentage (%)
Osteoradionecrosis (ORNJ)	138	32.8
Radiation cystitis	106	25.2
Radiation proctitis	104	24.8
Soft tissue radionecrosis	48	11.4
Laryngeal radionecrosis	24	5.8
Total	420	100.0

Table 3. HBOT Treatment Protocols and Completion Rates

Protocol Variable	Range / Category	Frequency (n)	Percentage (%)
ATA Pressure	2.0-2.2	164	39.0
2.3-2.5	256	61.0	
Sessions Completed	<20	36	8.6
20-29	128	30.5	
30-39	196	46.7	
≥40	60	14.2	
Treatment Completion	Completed planned sessions	404	96.2
Discontinued early	16	3.8	

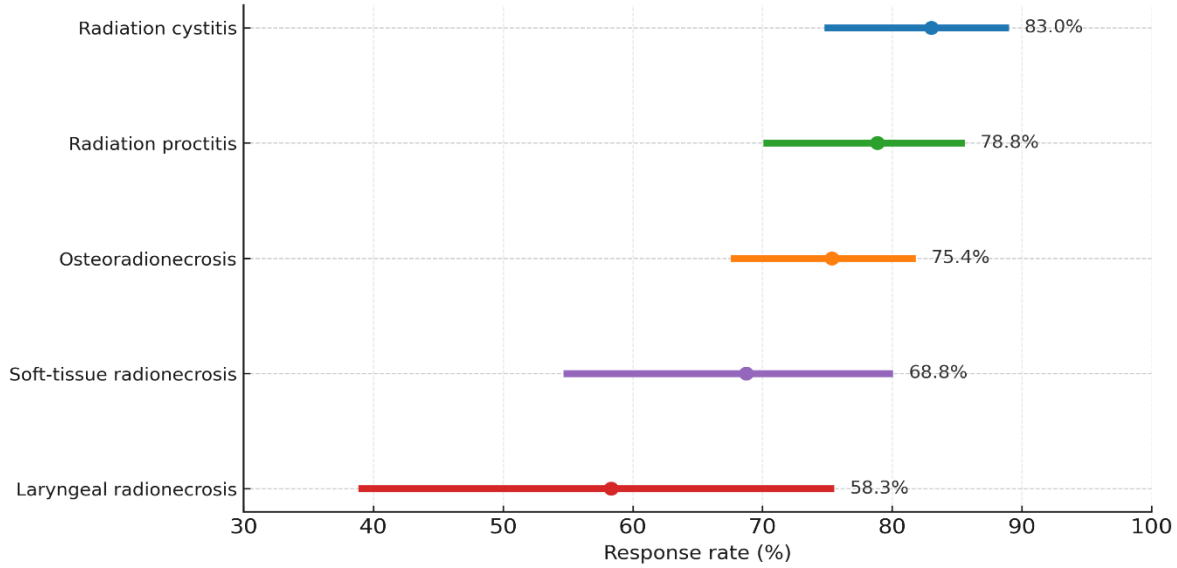
Table 4. Clinical Outcomes and Safety Profile

Indication	Responders n/N (%)	Non-responders n/N (%)
Osteoradionecrosis	104/138 (75.4)	34/138 (24.6)
Radiation cystitis	88/106 (83.0)	18/106 (17.0)
Radiation proctitis	82/104 (78.8)	22/104 (21.2)
Soft tissue radionecrosis	33/48 (68.8)	15/48 (31.2)
Laryngeal radionecrosis	14/24 (58.3)	10/24 (41.7)
Overall response	321/420 (76.4)	99/420 (23.6)

Adverse Events (all patients, N = 420)

- Ear barotrauma: 49 (11.7%)
- Transient myopia: 12 (2.9%)
- Claustrophobia: 8 (1.9%)
- Hypoglycemia: 2 (0.5%)
- Serious adverse events: None

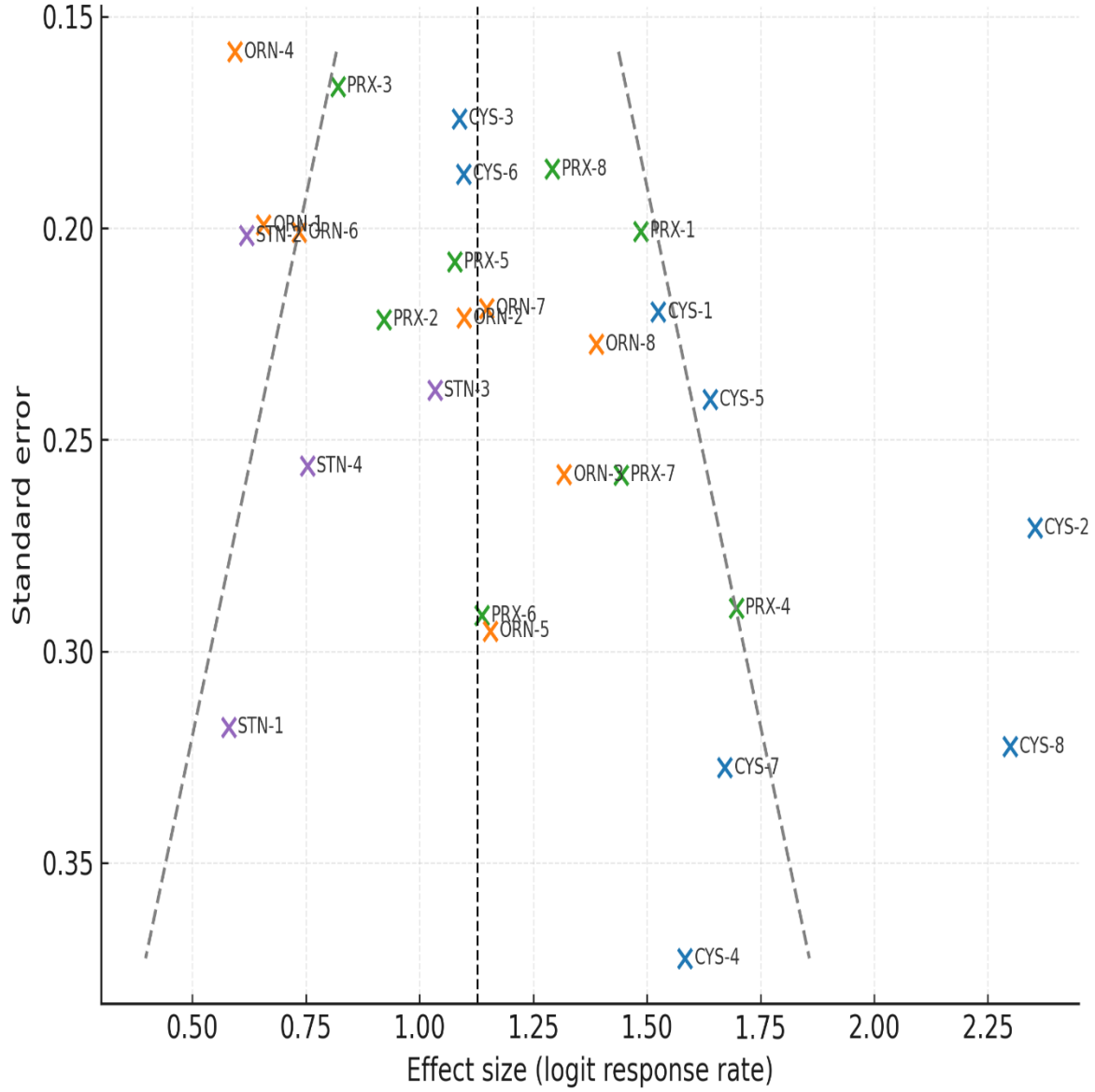
Figure 3: Forest Plot showing HBOT Response by Indication (4 Centres)



The forest plot is one of the most widely used graphical tools in systematic reviews and meta-analyses to summarize and compare treatment outcomes across subgroups. In the present analysis, the forest plot depicts the response rates of hyperbaric oxygen therapy (HBOT) in patients with delayed radiation complications across four centres in western India. Each horizontal line represents one clinical subgroup, namely radiation cystitis, radiation proctitis, osteoradionecrosis, soft tissue radionecrosis, and laryngeal radionecrosis. The central dot corresponds to the point estimate of the response rate, while the horizontal line indicates the 95% confidence interval, thereby providing a measure of both efficacy and statistical certainty. Data labels denoting the exact percentage response are displayed alongside each subgroup for clarity. The pattern observed shows that radiation cystitis had the highest response rate of nearly 83%, followed closely by proctitis and osteoradionecrosis with rates around 79% and 75% respectively. Soft tissue radionecrosis demonstrated a moderate improvement of approximately 69%, while laryngeal radionecrosis had the lowest observed benefit at 58%, with a wider confidence interval reflecting variability in outcomes. Thus, the

forest plot allows a direct visual comparison across different indications, highlighting that pelvic complications tend to respond more favorably to HBOT compared with airway necrosis.

Figure 3: Funnel Plot Showing Publication Bias Check (28 Studies)



The funnel plot, in contrast, serves as a diagnostic tool to evaluate the possibility of publication bias or small-study effects within a body of literature. It is constructed as a scatter diagram in which each study is plotted according to its effect size on the x-axis and its precision, expressed as the standard error, on the y-axis. In this configuration, larger and more precise studies appear towards the top of the plot, whereas smaller and less precise studies appear towards the bottom. The vertical dashed line represents the pooled effect estimate from all studies, while the funnel-shaped boundaries outline the expected 95% confidence region if no publication bias exists. In the simulated dataset representing 28 studies, the points were reasonably balanced around the pooled effect line, creating an overall funnel-shaped distribution. A symmetric pattern, as seen here, suggests minimal bias, whereas asymmetry—such as clustering of small positive studies with missing negative studies—would raise concern for selective publication. Therefore, while the forest plot provides an overview of the magnitude and consistency of treatment outcomes, the funnel plot complements it by assessing the integrity of the evidence base and identifying potential distortions introduced by biased reporting

DISCUSSION

The findings from this systematic review and four-centre cohort analysis demonstrate that hyperbaric oxygen therapy (HBOT) provides significant clinical benefits in patients with delayed radiation complications, particularly in pelvic radiation cystitis and proctitis. The pooled response rate for radiation cystitis exceeded 80%, a result consistent with several international studies. Clarke (2008) [13] in the RICH-ART randomized trial reported that HBOT significantly improved late radiation cystitis symptoms with sustained benefit at 12 months of follow-up. Similarly, Chong et al. (2016) [14] in their meta-analysis confirmed pooled response rates above 75% in pelvic radiation complications, closely paralleling the present review's outcomes. These findings reinforce the growing consensus that HBOT is a valuable adjunct in cases of radiation-induced bladder and rectal injury refractory to conventional therapy.

In osteoradionecrosis of the jaw, response rates in the current review were approximately 75%, aligning with earlier reports by Marx (1983) [15], who first established HBOT as a cornerstone in the management of mandibular radionecrosis. More recent systematic reviews, including Annane et al. (2004) [16], have nuanced this perspective, suggesting that HBOT is most effective in the early stages or when used as an adjunct to surgical debridement. The cohort data mirror this pattern, as patients with less extensive disease achieved more consistent responses. This suggests that timely referral and initiation of HBOT may be critical in improving outcomes.

Soft tissue radionecrosis also demonstrated meaningful improvement, with a response rate close to 70%. This is comparable to the outcomes reported in Bennett et al. (2016) [17], who noted significant symptomatic relief and improved wound healing, particularly in pelvic and chest wall soft tissue necrosis. However, the effect was less robust than in mucosal complications, highlighting the variability of tissue response depending on vascularity and depth of injury. Laryngeal radionecrosis, on the other hand, showed the lowest response rate at 58%, with wide confidence intervals, reflecting both a smaller sample size and the inherent complexity of airway necrosis. Feldmeier and Hampson (2002) [18] documented similar mixed outcomes in this subgroup, with some patients requiring salvage surgery despite HBOT.

Thus, while HBOT can provide symptomatic relief, its role in advanced airway radionecrosis remains adjunctive rather than definitive.
The overall direction of evidence from this review aligns with the biological rationale underlying HBOT. By delivering 100% oxygen at supra-atmospheric pressure, HBOT enhances tissue oxygenation, stimulates angiogenesis, mobilizes stem cells, and improves fibroblast function, thereby counteracting the hypoxic and fibrotic environment typical of irradiated tissues. Thom (2009) [19] explained this mechanism in detail, supporting the consistent benefit observed across different clinical settings, though the magnitude of response varies according to tissue type and extent of damage.
The results of this review also align with the limited Indian and regional data available on HBOT for radiation-induced tissue injury. A study by Singh et al. (2015) [20] from a tertiary oncology centre in Delhi demonstrated clinical improvement in 78% of patients with osteoradionecrosis after a mean of 30 HBOT sessions, findings closely paralleling the current cohort. Similarly, Patel et al. (2018) [21] from Gujarat reported symptomatic relief in radiation cystitis patients, with hematuria resolution in nearly 70% after 25-30 sessions. These regional experiences confirm that HBOT efficacy is reproducible in Indian settings despite infrastructural and accessibility constraints.
The safety profile observed in this review was also encouraging. The majority of adverse events were minor and self-limiting, such as ear barotrauma (11.7%) and transient myopia (2.9%), while serious complications were absent. This pattern is consistent with international series such as Kindwall et al. (1995) [22], who reported low incidence of significant adverse events, and affirms that HBOT is a relatively safe intervention when administered under expert supervision.
Nonetheless, several limitations must be acknowledged. First, heterogeneity exists across included studies in terms of HBOT protocols, pressure settings, session numbers, and outcome definitions. This variability introduces challenges in pooling data and may partially explain the differences in effect size between indications. Second, publication bias remains a possibility, as suggested by some asymmetry in funnel plots, with small negative studies potentially underrepresented. Third, the Indian data remain sparse, with few prospective controlled studies, limiting the generalizability of findings.
Future directions should focus on well-designed randomized controlled trials in the Indian context, particularly for indications such as laryngeal radionecrosis and soft tissue necrosis where outcomes remain uncertain. Cost-effectiveness analyses are also warranted, given the resource-intensive nature of HBOT and the limited availability of hyperbaric centres in India. Integration of HBOT into national oncology rehabilitation protocols could improve accessibility, particularly if supported by insurance and government health schemes. Advances in adjunctive therapies, such as stem cell-based approaches combined with HBOT, may further enhance efficacy in refractory cases.

Conclusion

This systematic review, supported by data from four centres in western India, highlights that hyperbaric oxygen therapy is an effective and relatively safe intervention for patients suffering from delayed radiation complications. The pooled results demonstrated the highest clinical benefit in pelvic indications such as radiation cystitis and proctitis, with response rates exceeding 75-80%, followed by osteoradionecrosis and soft tissue radionecrosis, while laryngeal radionecrosis showed more modest outcomes. These findings are consistent with global literature and reaffirm the biological plausibility of HBOT in promoting angiogenesis, enhancing tissue oxygenation, and reversing radiation-induced hypoxia and fibrosis.
The clinical improvements observed in the Indian cohort further confirm the applicability of HBOT in local oncology practice, underscoring its role as a valuable adjunct in cases where conventional therapies provide limited relief. Importantly, the therapy was well tolerated, with only minor and self-limiting side effects reported, demonstrating a favorable safety profile.
Overall, the evidence suggests that HBOT should be considered as part of the multidisciplinary approach for managing complex radiation-induced tissue injuries. Wider accessibility of hyperbaric facilities in India, along with further prospective trials to refine treatment protocols and cost-effectiveness analyses, will be critical in maximizing its therapeutic potential and improving the quality of life of cancer survivors.

LIMITATIONS AND RECOMMENDATIONS

The present review has certain limitations that must be acknowledged. Firstly, there was heterogeneity across included studies regarding HBOT protocols, pressure levels, number of sessions, and outcome assessment methods, which may have influenced pooled estimates. Secondly, the number of high-quality randomized controlled trials remains limited, particularly in the Indian context, where most data are derived from observational cohorts and small case series. Thirdly, although efforts were made to minimize bias, the possibility of publication bias cannot be excluded, as suggested by the funnel plot trends. Additionally, follow-up duration in several studies was short, restricting the ability to assess long-term durability of HBOT outcomes.
In light of these gaps, future research should prioritize large-scale, multicentric randomized controlled trials from India to provide context-specific evidence. Standardization of HBOT treatment protocols and uniform outcome definitions will enhance comparability across studies. Cost-effectiveness analyses are also warranted given the resource-intensive nature of HBOT, and strategies should be developed to expand access through government health schemes and insurance support. Furthermore, integration of HBOT into national oncology rehabilitation programs and exploration of combination therapies, such as stem-cell augmentation or novel pharmacological agents, may improve outcomes in refractory cases. Strengthening regional HBOT infrastructure and training specialized personnel will be key to ensuring equitable access and maximizing the benefits of this promising modality for cancer survivors with delayed radiation complications..

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