International Journal Dental and Medical Sciences Research
Volume 5, Issue 3, May - June 2023 pp 106-120www.ijdmsrjournal.com ISSN: 2582-6018

Consequential Fever of Post-operative Oral and Maxillofacial Surgery: A Systematic Review of Literature

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Date of Submission: 05-05-2023 Date of Acceptance: 15-05-2023

ABSTRACT

Background: Postoperative fever is one of the most common problems in oral and maxillofacial surgery (OMFS). Being a surgery of the head and neck region, OMFS calls for special attention. **Methods:**A comprehensive search of PubMed database, Dental and Oral Sciences Source and Web of Science was made for the literature of the last 20 years (2001-2020) using various keywords like 'Fever', 'Hyperthermia', 'Pathology of fever', 'Post-operative fever', 'fever-maxillofacial surgery' 'Fever - dental surgery', 'Fever-oral surgery', 'Fever-trauma' etc. The search yielded 90 relevant literatures for incorporation in this study.
Result: Publications on postoperative fever related to surgical site infection, sepsis, severe sepsis etc. are found significantly high in numbers in this search yield. Most of such infections were correlated with their odontogenic origin. Some rare but life-threatening hyperthermia case reports related to anaesthetics, adrenal insufficiency and thyroid storm are also found on record.**Conclusion:** Hyperpyrexia and hyperthermia need evidence-based treatment and hospital-based health-hygiene care.

Keywords: Postoperative fever; oral and maxillofacial surgery; Hyperpyrexia; Hyperthermia; hospital-based health hygiene; Systematic review

I. INTRODUCTION

Oral and maxillofacial surgery (OMFS) carries its importance in the head and neck sector. OMFS include surgical intervention of soft and hard tissue to address its disease and disorders. Reduction, reconstruction, aesthetic and cosmetic approaches are the underlying objective of OMFS. Both elective and emergency surgery for systemic and trauma cases are within the scope of OMFS.

Postoperative fever (POF) and pain in OMFS are common emergencies; even if it is reported up to 90% level. Body temperature is normal at 37 ^{o} C (98.6 ^{o} F) and temperature at 38 ^{o} C (100.4 ^{o} F) is fever. The onset of fever may be recorded during the procedure, soon after the surgery, or days after surgery attributing to some post-operational complicacy.[1,2]OMFS causes a considerable amount of tissue trauma and inflammation which in turn gives a platform for microbial infection. Thus cellular injury through systemic inflammatory response and infection promotes the production of pyrogenic cytokines, which trigger the febrile condition.[3,4] Pyrogenic cytokines or endogenous pyrogens are the peripheral mediators to induce fever.[5,6] Cytokines play important role in our immune response system and the protective responses of the immune system are found optimum at 39.5^{O} C.[7] Some pyrogenic cytokines are interleukins (ILs), tumour necrosis factor (TNF), interferon (INF) and granulocyte-macrophage colony-stimulating factor (GM-CSF). [7] Biosynthesis of prostaglandins is enhanced at the organum vasculosum of the lamina terminalis (OVLT) in the brain by the effect of these cytokines and which play as the central mediator to induce fever.[8]Sometimes specific anaesthetics, blood transfusion, drug intolerance, and hormonal crisis may also cause the potential life-threatening hyperthermia during the procedure or immediate post-surgical period.[9-11]Surgery may also be a coincidence to the underlying brain injury, viral infection, systemic inflammatory response, sepsis, severe sepsis or even septic shock which can present a fever during or after the surgical procedur[12]. The present study is a systematic review of literatures on postoperative fever (POF) with special reference to the oral and maxillofacial sectors. A systematic search of published literature on the subject from 2001 to 2020 was performed and incorporated into the study. As a special mention, this study includes several typical scenarios and rare case reports in OMFS, which are critically reviewed and correlated with evidence-based pathophysiology.

International Journal Dental and Medical Sciences Research
Volume 5, Issue 3, May - June 2023 pp 106-120www.ijdmsrjournal.com ISSN: 2582-6018

II. METHOD

The present systematic review on the consequential fever of post-operative oral and maxillofacial surgery (OMFS) is based on the published data about the subject. A comprehensive search of PubMed database, Dental and Oral Sciences Source, Web of Science etc. for the last 20 years (2001-2020) was done using various keywords and their combinations like 'fever', 'hyperthermia', 'pathology- fever', 'post-operative fever', 'fever - maxillofacial surgery', 'fever - dental surgery

'Fever-oral surgery', 'fever-trauma'. In addition, the search included anaesthesia and pain management, dentoalveolar surgery, orthognathic surgery, cleft and cosmetic surgery, reconstruction; facial trauma and bone fracture. Literatures were also searched manually by library consultation. Publications in the form of abstracts, proceedings, editorial columns and other grey literatures were not in the selection criteria. Non-English and non-human publications were also discarded. Mostly critical review, cohort study, case report, management protocols etc were focused on for this study. Literatures that met the selection criteria are put under different year classes, aetiology and treatment management groups for review.

III. RESULT

The search yielded 124 articles, 90 of which met the inclusion criteria. In this systematic review major information, findings and synthesis are described under different sub-headings, flow charts, figures and tables as mentioned below. A schematic chart is developed for the interpretation of fever aetiology and its mechanism at a glance (Figure 1).

Analysis of search yield

There is an increasing number of literature found over each five years class during the last twenty years (Figure 2). The incorporated publications are broadly classified into four categories viz. i) Fever history and basic science (FHBS), ii) Review-post operative fever (RPOF), iii) Review and cohort study of fever after maxillofacial surgery (RCFMS) and iv) Case reports of fever after maxillofacial surgery (CRFM). The percentage of contribution of such literature for this review is given below (Figure 3). The case studies of POF in OMFS are further categorised based on the aetiology as presented in Figure 4. The findings of the review are presented as important terminology, principle, pathways, mechanism, classification, aetiology, epidemiology, evaluation and management of POF in OMFS.

Pyrexia, Hyperpyrexia and Hyperthermia.

Human body temperature at 37^{o} C(98.6^{o} F) is consensually accepted as the average normal temperature. A significant rise in body temperature over its normal range is considered fever (Table 1). POF has been described in the literature as pyrexia, hyperpyrexia and malignant hyperthermia. Although hyperpyrexia and hyperthermia result in high elevated temperature, are different (Table 2). Factors that are responsible for the onset of pyrexia are known as a pyrogen. Neuroleptic malignant syndrome (NMS), malignant hyperthermia(MH) thyroid storm, adrenal insufficiency etc. are examples of some high-risk hyperthermia conditions of a medical emergency.[13-15]

Pyrogens

Pyrogens are substances that induce pyrexia or febrile response. Pyrogens are further classified as exogenous and endogenous. Exogenous pyrogens are generally microbial in origin. These are lipopolysaccharide (LPS) endotoxin of the outer cell membrane in gram-negative and peptidoglycan of the cell wall of gram-negative and gram-positive bacteria. Killed or live viruses and fungal elements are also considered exogenous pyrogens. Non-microbial exogenous pyrogenic factors include selected antigens, drugs, and steroids of individual susceptibility. Endogenous pyrogens are specific immune regulatory proteins, known as cytokines produced in the host body in response to exogenous pyrogens or some metabolic disorders. Some of the cytokines such as interleukins (ILs), tumour necrosis factor (TNF) and interferon (INF) are considered the major endogenous pyrogens of different pyrogenicity (Table 3).[5-8]

Principle and pathways of fever

The endogenous pyrogen as an immune signalling system stimulates prostaglandin formation in the hypothalamic preoptic area which shifts the new set point of body temperature and causes fever.[16] The immune signalling pyrogens are carried to the hypothalamus by the vascular system or through peripheral nerve fibre transmission.

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Infection or inflammation mostly stimulates monocytes/macrophages and neutrophils to produce a cascade of cytokines which are released into the circulation. In this cytokine cascade tumour necrosis factor-alpha (TNF-α) is appeared initially in the circulation followed by interleukin- 1ß (IL-1ß), interleukin-6 (IL-6), macrophage inflammatory protein-1 (MIP-1) *etc*. However, among these cytokines, IL-6 is detected in higher quantity.[17,18]The cascade is also triggered in response to superantigen peptidoglycans or muramyl dipeptides of Gram-positive and Gram-negative bacteria. Similarly, viral infection or administration of any viral product can activate the cytokine cascade initiated by interferon. The cascade of pyrogens is dominated by interleukin-6 (IL-6), as the endogenous humoral signals reach the brain by the vascular system. The Organum Vasculosum of the Lamina Terminalis (OVLT) and the subfornical organ (SFO) are the circumventricular organs where specific neurons/glial cells respond to circulating pyrogens and produce prostaglandin (PG) as the central or secondary mediator in fever pathway. Some receptors on endothelial cells also respond to the endogenous pyrogen to produce PG. PGE_2 the specific prostaglandin seems to be the end player in the fever pathway for an upshift of a thermal set point in the hypothalamus.[8,19,20]Apart from the circulating pathway, the stimuli of pro-inflammatory cytokines and endo-toxin can also be transmitted through afferent neural pathways.[7,12] The production of PGE_2 is a function of the enzyme cyclooxygenase (COX).[17]

Mechanism of antipyretics action

Acetaminophen products (antipyretics) reduce the synthesis of prostaglandin by inhibiting the cyclooxygenase (COX) in the arachidonic acid metabolism pathway to bring down the production of PGE_2 and temperature set point at the hypothalamus. It also acts on the serotonergic pathway to reduce pain.[22]Non-steroidal anti-inflammatory drugs (NSAIDs) are the therapeutics commonly used for inflammatory conditions of trauma, injury and systemic disorders. NSAIDs act on the arachidonic acid pathway to reduce inflammation pain, and fevermostly mediated byCOX inhibition.[23] Antibiotic prophylaxis and therapy reduce the microbial population and thus control the pyrogenic cytokines pool responsible for fever development.[24]

Postoperative fever in oral and maxillofacial surgery

POF and pain in OMFS are common phenomena**.** In this review, POF cases and cohort studies are discussed in the context of W's principle, infectious and non-infectious, surgery-related and non-related *etc*. (Table-4 and 5). A school of surgeons also classify the emergence of fever as immediate, acute, sub-acute and delayed category (Table-6). POF following OMFS attributing to the drug reactions are also found and reviewed (Table-7). A consolidated list of life-threatening high-risk fevers following OMFS has been worked out (Table- 8). Some potential fever-producing pathogens that are identified from the wound and infection of OMFS case studies are annexed (Table-9). Moreover, some of the important case reports are produced in a tabular format for easy and instant perusal (Table- 10).

IV. CONCLUSION

Mild to moderate fever during the first 2 days of the procedure may not be that important to draw the attention of the surgeon. A lot many POF in OMFS is due to the odontogenic origin and causes hyperpyrexia. Hyperpyrexia and hyperthermia are not synonyms but promote extremely high body temperature. Hyperpyrexia and hyperthermia in OMFS irrespective of their aetiology are of high risk and life-threatening. These fevers need an immediate diagnosis for their aetiology for treatment and hospital-based care. The present study shows over the year increasing trend in understanding the principle, aetiology and epidemiology of some potentially fatal complications in OMFS.

Conflicts of Interests: The authors declare that they do not have any conflicts of interests.

Ethical approval: this article does not require any ethical approval.

Funding: No funding received

Authors contribution:AAR, SPL and SM conceptualized the data. AAR collected the data and drafted the manuscript. SM, SP and SKM critically evaluated the manuscript.

International Journal Dental and Medical Sciences Research
Volume 5, Issue 3, May - June 2023 pp 106-120www.ijdmsrjournal.com ISSN: 2582-6018

Table 1: Classification of POF based on temperature curve and grades in OMFS.

Grade of fever	Temperature range	Some important citations
Normal	98.6 °F (37 ° C)	
Low pyrexia	Up to100.4 ° F (38 ° C)	Pal and Acharee[1], Abdelmaseeh*et al.*[2], Reifenstahl& Rowshan[9],Ansari[19] Rosenberg *et al.*[25]
Moderate pyrexia	Up to 102.2 °F (39).	
High pyrexia	Up to 105. 8 ° F (41°F)	
Hyperpyrexia,	Above 106 °F (41.1C)	
Malignant Hyperthermia	Above 106.7 ° F (41.5 ° C)	

Table 2: Difference between fever and hyperthermia during the perioperative period.

Hyperpyrexia[3,7, 12]	**Malignant Hyperthermia** [9,15,25, 26]
Temperature cannot climb up persistently. Fever is regulated at the hypothalamic centre as a 'set point regulator'.	No hypothalamic 'set point' is involved. Temperature rise has no set limitation.
Production of PGE2 is influenced by the microbial toxin, endotoxin, and pyrogenic cytokines (IL1b, IL6, TNFα, INF etc.). Tissue trauma, inflammationSSI, drug reaction and other nosocomial infections cause postoperative fever.	Rise of body temperature caused by the influence of some specific, drugs, anaesthetics, surge or insufficiency of hormones, syndromes (Malignant hyperthermia, Neuroleptic malignant syndrome, Serotonin syndrome etc.) and heat stress (environmental).
Generally, body temperature rises to 41° C (106°F)	The sudden rise of temperature beyond 40° C (104°F). Consistently increases 1-2° F at a small time interval.
It May not be life-threatening but need intervention to reduce the temperature	Always life-threatening need immediate aggressive intervention
Antipyretic drugs regulate the production of PGE2 and bring down the 'set point' to reduce body temperature	Antipyretic drugs cannot reduce body temperature. Identification of the underlying cause of hyperthermia and specific drug withdrawal intervention may reduce the temp. Cool damp sponging, physical application of cool fluid etc. may reduce the temperature instantly.

Table 3: A comparative account of pyrogenic activity for different cytokines.

Nam of cytokines	**Fever-inducing dose (minimum effective dose)**	**Pyrogenic activity**	**Pyrogenic properties**	**Reference Index**
IL1ß	1-10 ng/kg	++++	Most potent pyrogen	Dinarello[5] El-Radh*et al.*[7] Netea*et al.*[8] Sattari*et al.*[17]
IL1 α	1-10 ng/kg	++++		
IL6	1000-10000ng/kg	+++	Found distally to TNF and IL1 in cytokine cascade	
TNF α	200-500 ng/kg	+++	TNFa induces IL1	
INF α	0.1 0.5 microg/kg	++	INF α is more potent	
INF ß	0.1 0.5 microg/kg	++	INF ß less potent	

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Table 4: Seven W's classification of POF found in OMFS case studies.

Five W's	Diagnosis	POD	INF/NIF	Some important citations
Wind	Atelectasis	1-3	NIF	Pal and Acharee[1];Abdelmaseeh*et al.*[2]; Maday*et al.*[3] Narayan and Medinilla[12]; Ansari [19] Jadwani*et al.*[27] Mavros*et al.*[28] Wang *et al.*[29] Assael[30]
	Pulmonary embolus	5-7	NIF	
	Pneumonia	3-5	INF	
	Tracheal intubation		INF	
Water	Urinary tract infection	2-3	INF	
Wound	Necrotising soft-tissue infection (NSTI)	3-7	INF	
	Surgical sitter infection (SSI)	5-7	INF	
	Catheters and prostheses relate to infection	3-5	INF	
Walking	Deep vein thrombosis (DVT)/ Thrombophlebitis	5-7	NIF	
Wonder drugs	Iatrogenic	Days- weeks	NIF	
Withdrawal	Delirium tremens (DTs)	3-5	NIF	
'Wonky' glands	Adrenal insufficiency	0-1	NIF	
	Thyroid Strom	0-2	NIF	

Table 5: POF is related to surgery (SR) and not related to surgery (SN) in OMFS cases.

Etiology of POF	Category	Grade of fever	Some important citations
Pneumonia,	SR	Medium-High	Ohba*et al.*[31];Cristabel*et al.*[32]
Surgical trauma	SR	Low-medium	Taher and Bede[33];Miyaoka *et al.* [34]
UTI/IRI	SR	Medium-High	Ansari [19];Jadwani*et al.*[27]
Infected incision	SR	Low-medium	Okechi*et al.*[35]; Liang *et al.*[36]
Abscess	SR	Low-medium	Serra *et al.*[37]; Reinholdtand Klug[38]
Sepsis/severe sepsis	SR	Medium-High	Mokart*et al.*[39]; Moss *etal.*[40]
Blood transfusion	SN	Medium-High	Park *et al.*[11];Neswi*et al.*[41];
DVT	SN	Low-medium	Lodders et al [42] Babu etal[43]
Osteomyelitis	SR	Medium-High	Nelke*et al.*[44]; Humber*et al.*[45]
Anesthetic-hyperthermia	SN	High	Patil[14]; Herlich[46]
Toxic shock syndrome	SR	High	Aquino *et al.*[47]
Prosthetics (miniplate, screw)	SR	Low-medium	Lim *et al.*[48]; Rosa*et al.*[49]
Ludwig's angina	SR	Medium-High	Carter and Lowis[50]
Common systemic viral/bacterial/parasitic fever	SN	Low-high	Ansari [19] Jadwani*et al.*[27] , Christabel *et al.*[32]
Neuroleptic fever	SN	Medium-High	Shimada *et al.*[13];Herlich[46]
Immunocompromised fever	SN	Medium-High	Ansari [19]
Alcohol withdrawal fever	SN	Low-medium	Jadwni*et al.*[27]; Christabel *et al.*[32]
Fracture reduction	SR	Low -medium	Metsemakers*et al.*[51]; Gordon *et a.*[52]
Otitis media,	SN	Low-medium	Jadwani*et al.*[27] ; Christabel *et al.*[32]

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Table 6: Recent classification for POF found in OMFS case studies.

Days	Category	Disease/disorder	Some important citations
0-1	Immediate fever	Anaesthetic hyperthermia, adrenal insufficiency non-hemolytic transfusion reaction, Ludwig's angina	Gibbs *et al.*[10]; Park*et al.*[11];Lim et al.[48,] Verstraete*et al.*[53]; Tejaswi and Subash[54];Boffano*et al.*[55]; Um *et al.*[56]; Yao *et al.*[57]; Tian-Guo *et al.*[58]; Guru *et al.*[59]; Davis *et al.*[60]; Pochana and Sessirisombat[61]; Samieirad*et al.*[62]; Badri, *et al.*[63]; Abbaszadeh and Sheibani[64] Gilbertson *et al.*[65]; Adesina *et al.*[66]
1-7	Acute fever	Atelectasis, aspiration pneumonia, obstructive pulmonary embolism, odontogenic infection, sepsis, multi-space infection, osteotomy, surgical site infection Nosocomial infection, infection	
8-28	Sub-acute fever	Deep vein thrombosis,iatrogenic	

Table 7: Drug-related fever after oral and maxillofacial surgery (Ansari[19]; Christabel *et al.* [32])

Drug category	**Drugs**
Antimicrobials	Penicillin G, Ampicillin, Cephalosporins, Tetracycline, Sulfonamide, Isoniazid, Fluoroquinolones, Vancomycin, Rifampin, Nitrofurantoin, Amphotericin B,
Cardiovascular	Alpha methyldopa, Quinidine, procainamide, hydralazine, Nifedipine Thiazide diuretics, Furosemide, Spironolactone
Anticonvulsant	Phenytoin
Anesthetic/sedative/analgesics	Barbiturates, Salicylates, Cocaine, Halothane, Nonsteroidal anti-inflammatory drugs (NSAIDS), Procainamide
Central Nervous System	Carbamazepine, phenytoin, Chlorpromazine, Haloperidol, Riamterene, Atropine, Barbiturates
Others	Cimetidine, Metoclopramide, Allopurinol, Interferon, Propylthiouracil, Iodides, Heparin (especially unfractionated), Antihistamine, Hydroxyurea, Heparin, Immunoglobulins, Mycophenolate mofetil, Propylthiouracil

Table 8: Life-threatening high-risk fever recorded in oral and maxillofacial surgery.

High-risk fever	Clinical clues for diagnosis	Some important citations
Myonecrosis (Clostridium sp.)	Cause tissue death, decay and gas formation in trauma and surgical site wound, multiple fracture sites. fever, fatigue, painful or tender hardedematous affected area, foul- discharge,	Davis *et al.*[60]; Pochana and Sessirisombat[61] ;Song *et al.*[67]; Gamoh*et al.*[68]; Cousin *et al.*[69]
Necrotizing fasciitis (flesh-eating infection)	Soft tissue infection with severe pain, fever with chills and sweating, nausea, dizziness, and infrequent urination.	Hechlerand Blakey[70]; Abe *et al.*[71]; Arruda *et al.*[72]

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Sepsis (sepsis, severe sepsis, and toxic shock)	Sepsis: Fever >101ºF or a temperature < 96.8ºF tachypnea and tachycardia. Severe sepsis: low platelet count, decreased urination, problems breathing, abnormal heart functions, chills and fall of temperature, unconsciousness Septic shock: severe sepsis with fall in blood pressure	Christabel *et al.*[32]; Mokart*et al.*[39]; Moss *et al.*[40]; Aquino *et al.*[47]; Carter and Lowis[50]; Tian-Guo *et al.*[58]; Falconer*et al.*[73] ;Handley *et al.*[74]
Pulmonary embolism	Shortness of breath, chest pain, profuse sweating, Cough irregular heartbeat, fever,	Wang*et al.*[29]; Borges*et al.*[75]; Forouzanfar*et al.*[76]; Valid and Tenens [77]
Serotonin syndrome	High body temp. (106.0 °F) increased reflex, sweating, dilatedpupils, seizures and extensive muscle breakdown	Szakaly and Strauss[13]
Malignant hyperthermia	Hypercapnia, tachypnea, tachycardia, muscle rigidity or spasm.Extremely high temperature	Reifenstahi and Rowshan[9]; Gibbs *et al.*[10]; Patil [14] ; Herlich[46]
Neuroleptic malignant syndrome	High fever (102-104° F), irregular pulse, muscle rigidity tachypnea, tachycardia, autonomic nervous system dysfunction	Jadwani*et al.*[27] ; Shimada *et al.*[78]
Delirium treatments	The onset of confusion with shaking, shivering, irregular heart rate, and sweating. Appears after 3 days of alcohol withdrawal.	Ansari [19] Christabel *et al.*[32]; Pile[79]
Adrenal insufficiency	Hypotension, tachycardia, hypoxia, and fever mimic,ionic disbalances, fever, chills, sweating, confusion, slurred speech, hypoglycemia	Khalaf *et al.*[26]; Jadwani*et al.*[27]
Thyroid storm.	High systolic and low diastolic blood pressure, high fever, diarrhoea, vomiting, terrible anxiety, nervousness and confusion, unconsciousness	Weinstock *et al.*[15]; Ansari [19]; Christabel *et al.*[32]

Table 9: Potential fever-producing pathogens identified from the wound and infection of OMFS.

Bacteria Category	Generic and species name	Some important citations
Gram-negative anaerobic	Clostridium perfringensClostridium septicum , Bacteroides fragilis	Assael[30]; Christabel *et al.*[32] Reinholdt and Klug [38] Tian-Guo *et al.*[58]; Guru *et al.*[59] ; Badri*et al.*[63]; Song *etal.*[67];Hechlerand Blakey[70] ; Abe *et al.*[71] Reichman and Greenberg [80]; Negi*et al.*[81];Kaya*et al.*[82]
Gram-negative facultative anaerobic	Escherichia coli,Pseudomonas aeruginosa, Klebsiella aerogenes, Klebsiella oxytoca, Citrobacter freundii, Citrobacterkoseri, Proteus mirabilis, Proteus vulgaris	
Gram-positive facultative anaerobic	Enterococcus faecalis, Streptococcus pyogenes, Streptococcus pneumonia, Staphyloccous epidermis	
gram-positive facultative aerobic	Staphylococcus aureus, Klebsiella pneumoniae, Klebsiella oxytoca	

Gram-negetive facultative aerobeic	Aeromonas hydrophila	
Gram-negative aerobeic	Acinetobacter baumannii, Acinetobacter lowfii	
Fungal	Candida albicans ,Candida tropicalis, Candida glabrata, Cladosporium cladosporioides Cladosporium haerospermum, Cladosporium oxysporum	

Table 10: A Concise and consolidated sheet on some of the case studies of POF in OMFS.

Author(s)	Type of surgery	Male/Female	Duration of Fever	Correlation
Aframian-Farnad (2002)[83]	maxillomandibular fixation	24	Not significant in all cases	Postoperative atelectasis
Nakano *et al.*(2003) [84]	Radical sinus, Cyst excision, Open fracture reduction	12(7/5)	1-3 days fever	Correlated IL-6 levels in day1-day 3
Miyaoka *et al.* (2005) [34]	Jaw osteotomy with prognathism	21(6/15)	1-3 days fever	Correlated with circulatingIL-6 and IL-10
Carter and Lowis (2007) [50]	Drainage for Submental/subman dibular cellulitis	1(1/0)	3 days fever	Death correlated with Ludwig's angina &odontogenic sepsis
Cutilli*etal.* (2007)[85]	Dental surgery	1(0/1)	Hyperpyrexia for few days	Necrotizing fasciitis of the maxillofacial region
Serra *et al.* (2009) [37]	Facial trauma and orbital abscess	01(0/1)	Moderate fever for 5 days	Orbital cellulites and abscess
Aziz *et al.* (2010)[86]	Orthognathic Surgery	01(0/1)	Moderate fever for 2 days	Post-operative lobar collapse
Gordon *et al.* (2011)[52]	Mandibular fracture	44(36/8)	Fever and pain varied with fracture severity	Fracture severity and post-operative inflammatory complications (POIcs)
Moss et al. (2012)[40]	Third molar extraction	1(1/0)	Fever and pain	correlated with Jarisch–Herxheimer like reaction
Babu *et al.*(2013) [43]	Mandibular fracture reducton	2(1/1)	Moderate fever	Post-surgery DVT
Song *et al.*(2014) [67]	Dental infection	1(0/1)	Moderate fever for a few days	Necrotizing Fasciitis and myositis in the buccal and terygomandibular spaces
Nelke*et al.* (2015) [44]	Orthognathic surgery	1(0/1)	Moderate fever for a few 3 days	Osteomyelitis in the facial bone
Lodder*set al.*(2015)[42]	Oncological OMFS	226	Moderate fever for a variable period	venous thromboembolis

				m (VTE)
Maciaget *al.* (2016).[87]	Lingual frenulectomy	1(1/0)	Slow fever and pain	Correlated with Ludwig's angina
Davis *et al.* (2016)[60]	Orthognathic surgery	143	Infection &fever 11 to 15days	Surgical site infection
Prathapet *al.* (2016)[88]	Extraction of the third molar	1(0/1)	For few days	chronic osteomyelitis and bone necrosis
Yao *et al.* (2017)[57]	Onco surgery and reconstruction	84	SSI and POF within 30 days	SSI and plate exposure
Um *et al.* (2018) [56]	Abscess in the maxillofacial area	1(1/0)	Slow to moderate fever	Obstruction atelectasis
Gibbs *et al.* (2019).[10]	Maxillofacial trauma	1(1/0)	Hyper metabolism due to anaesthesia	Malignant hyperthermia
Samieiradet *al.* (2018)[62]	Orthognathic surgery	1(0/1)	After 7 days	Correlated with Post-surgery DVT
Aquino *et al.* (2019) [47]	Third molar extraction	1(1/0)	Intermittent POF up to 4 weeks	Toxic shock-like syndrome
Prabhu *et al* (2019) [89]	Mandibular and lingual surgery	890 (563/327)	Fever, swelling Ludwig's angina	Acute facial space infection Streptococcus, Staphylococcus
Guru *et al.* (2019) [59]	Cancer, tumours, Cleft palate, Orthognathic	25(16/9)	Fever after 2 days	Hospital-acquired SSI, UTI, BSI
Okchiet *al.* (2019)[35]	Cyst enucleation, Fracture reduction, tumour excision	23	1-5days	Postoperative tissue injury
Verstraeteet *al.* (2019)[53]	Bimaxillary orthognathic surgery	1(0/1)	2 days	Atelectasis and bilateral pneumothorax
Tian-Guo *et al.* (2019)[58]	Dental cavity infection	01(1/0)	10 days and death	Odontogenic infection, multi-space infection, septic shock, MOD
Badri, *et al.* (2020)[63]	Mandibular fracture reduction	1(1/0)	Few days	Cervical necrotizing fasciitis (Staphylococcus sp.)
Cousin *et al.* (2020)[69]	Orthognathic surgery	41(18/23)	Infection and fever within 25 days	Surgical site infection SSI
Taher and Bede (2020)[33]	Third molar impaction	39(12/27)	1-3 days	Correlated to Interleukin-6
Liu *et al.* (2020) [90]	OMFS free fibula flap reconstruction	160	Varied with severity	Postoperative pulmonary complication

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Volume 5, Issue 3, May - June 2023 pp 106-120www.ijdmsrjournal.com ISSN: 2582-6018

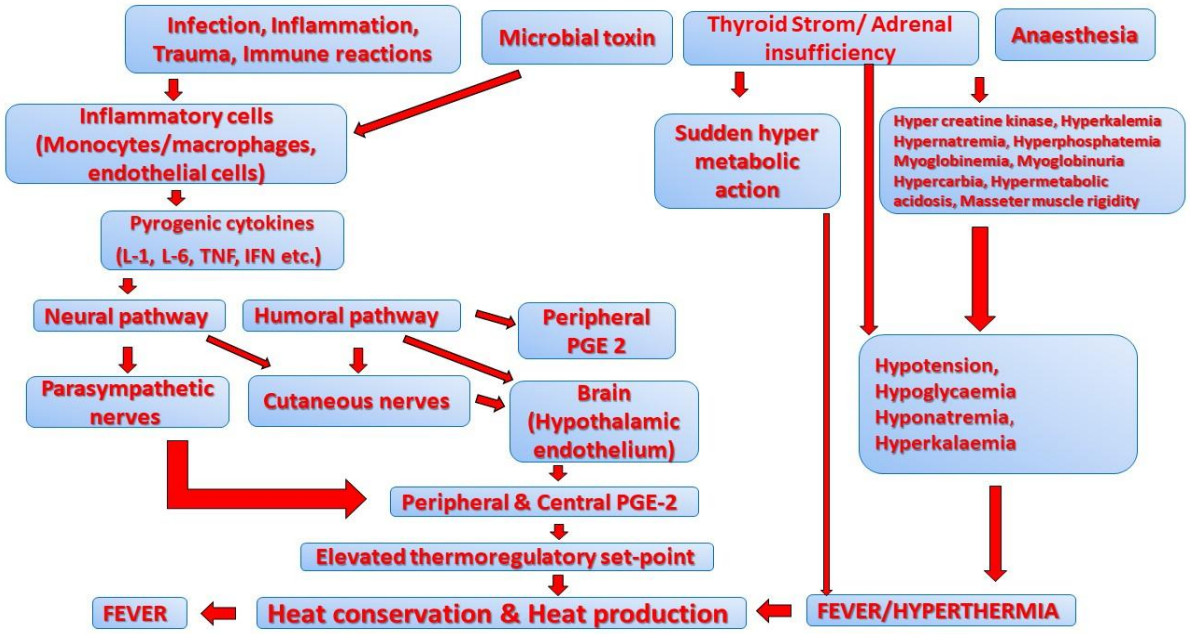

Figure 1. Consolidated chart showing the pathophysiology of POF in OMFS

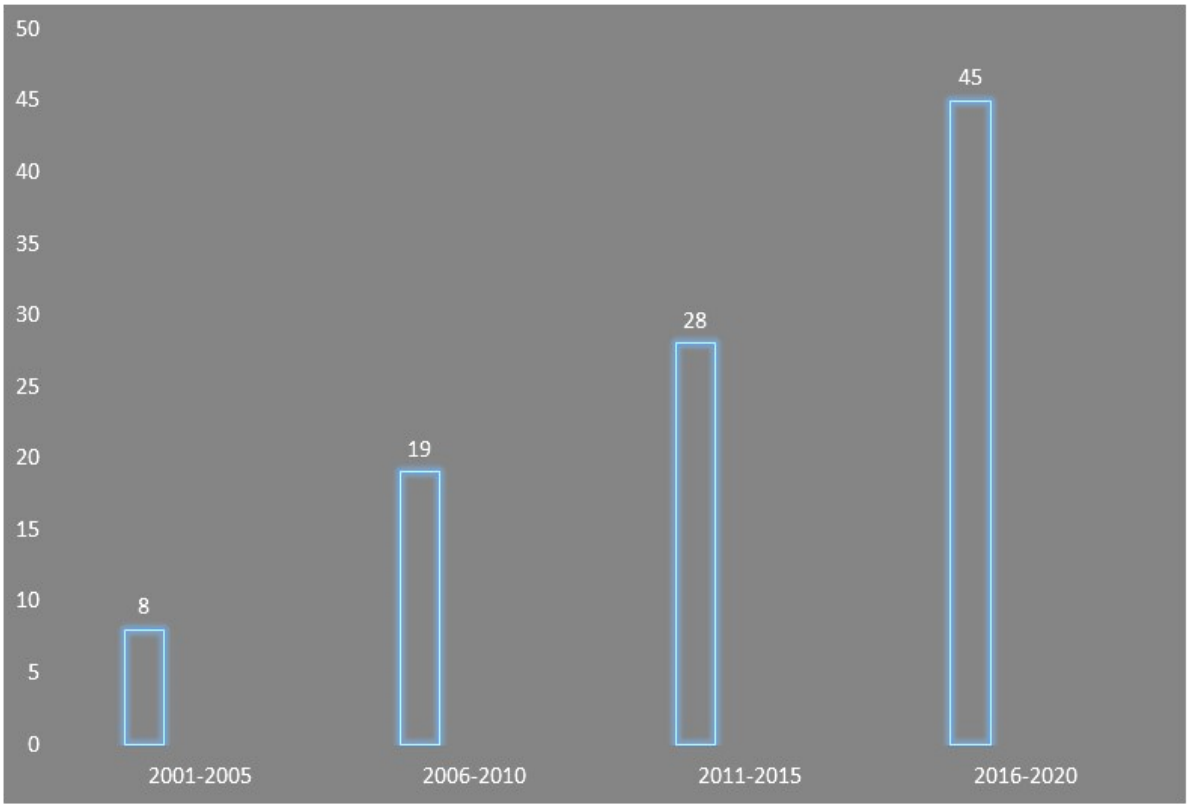

Figure 2. Five-yearly groups of literature and their % of incorporation in this review

International Journal Dental and Medical Sciences Research
Volume 5, Issue 3, May - June 2023 pp 106-120www.ijdmsrjournal.com ISSN: 2582-6018

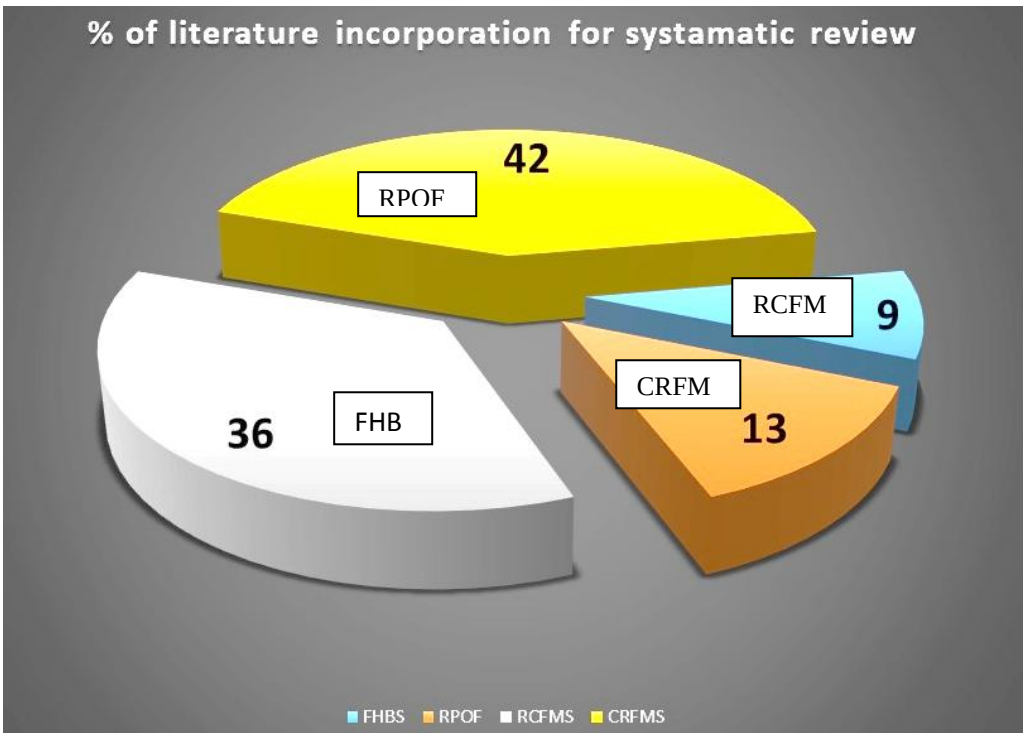

Figure 3. Different categories of literature incorporated in this study

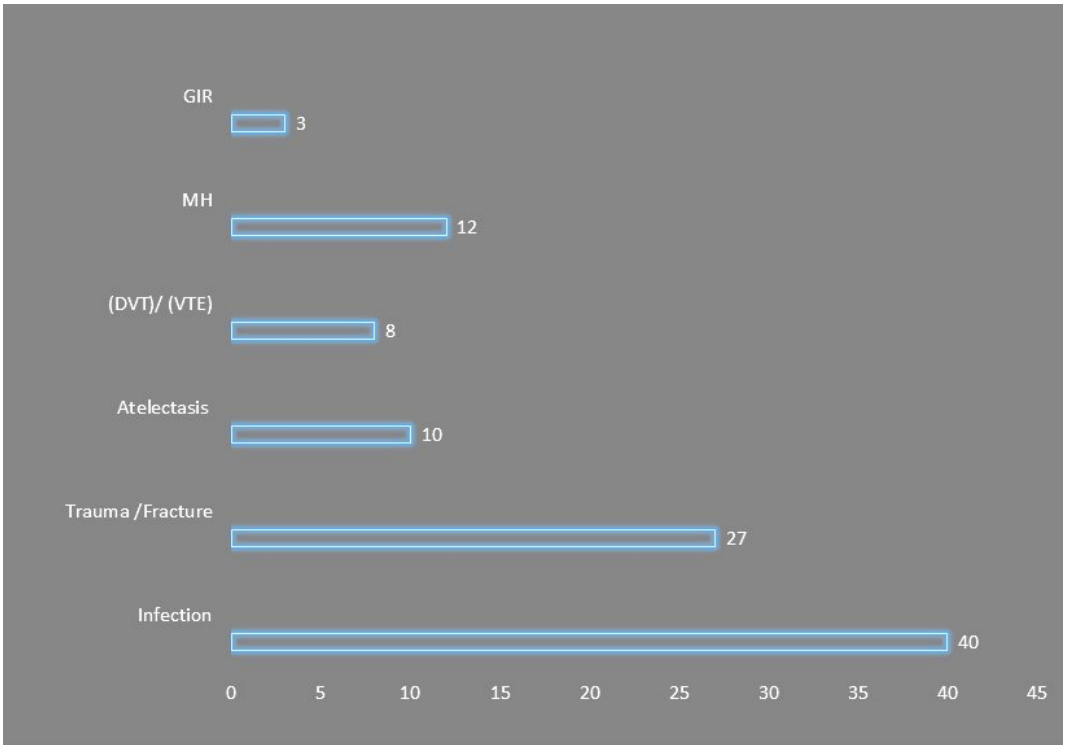

Figure 4. Case studies supporting different aetiologies of POF in this review (%)

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