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The hidden burden: A review of toxicity from femoral orthopedic implants

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ABSTRACT

Locomotion is one of the essential characters of humans. During daily activity human body is subjected to several factors such as shock, stress, strain and other environmental factors. Most of times human body remains un-affected by these factors as they are contradicted by skin, fats, muscles, bones etc. But when the body is subjected to a trauma of higher impact an injury can occur which can affect capability of human body. One of the common injuries is bone fractures. Among the bone's femur is susceptible to the fractures being the longest bone in the human body. Femoral fractures affect mobility of humans to the greater extent; in order to restore maximum function of femur, implants are used to treat fractures. Implants such as nails, Screws, plates are used to repair the bone. These implants are either made up of metals or alloys commonly used metals are titanium, gold, iron, cobalt, chromium and several others that have been reported to cause one or other toxicological episodes. Femoral fractures may take months to get treated and till the time implants are embedded in human body. Within this time frame implants start producing oxides that may result in several implications such as hypersensitivity, allergies, neurological problems and other toxicological implications.

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INTRODUCTION

Femoral shaft fractures are a common orthopedic injury due to high impact trauma. The incidence of femoral shaft fracture ranges between 10 and 21 per 100,000 per year and out of these 2 percent are open fractures. The most common etiological factor is due to high or low energy mechanisms, most commonly caused by automobile accidents and falls from height. Low energy impact injuries are more common in elderly population suffering from osteoporosis (Ghouri *et al.*, 2023). Common femoral factures are indicated in (Fig. 1).

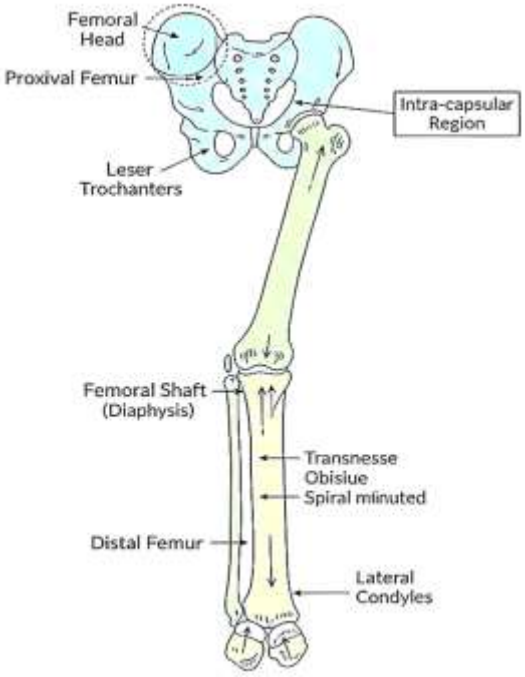

Fig. 1. Regions prone to femoral fracture

There has been 1-9 % incidence of proximal femur fractures (femur head and neck and intertrochanteric) associated with femur shaft fractures and 20-50% of such associated fractures go unnoticed. Such associated fractures should be investigated thoroughly as they are clinically important for further management. Intramedullary nailing is the gold standard for the treatment of femoral shaft fractures. Along with the femoral shaft fractures, there is another type of femoral fracture closely associated with implants in their management. These are the femoral neck fractures which is a type of intra-capsular hip fracture. The femoral neck is the connection between the femoral head and the shaft; the head of femur articulates with the acetabulum therefore this junctional location makes the neck of femur prone to fractures. Results of annual census indicate that out of 1.6 million hip fractures annually, 70 percent of these fractures occur in women indicating a strong correlation between female gender and hip fractures (Osteoporosis Canada, 2021). Other risk factors include osteoporosis and decreased mobility. The management of such fractures depends on several factors such as Age, Displacement of fracture etc. Elderly patients with displaced fracture either undergo Hemiarthroplasty or Total hip arthroplasty depending upon their baseline activity level and age (Sansone *et al.*, 2013).

Orthopedic implants are broadly divided into Permanent, including hip, knee, ankle, shoulder, elbow wrists and finger joints, and Temporary including wires, screws, plates and intra-medullary nails. Metallic alloys, ceramic and polymers are the principal compositional part of such implants (Ghouri *et al.*, 2023; Al-Shalawi *et al.*, 2023).

Titanium alloys are most commonly used in the production of orthopedic implants such as intramedullary nails and total hip femoral stem (Jacobs *et al.*, 2001). The reason for this is that Titanium has the key properties desirable for any implanted material in the body, which is resistance to metabolism by the body and to the oxidative processes therefore not leading to production of any active metabolites. Titanium when used as an implant leads to form a thin oxidative film over the implant which is biologically inert. Stainless steel is also a component of choice in various implants and has been the earliest modern implant being used worldwide. The most commonly used alloy is 316L composed of iron, chromium, nickel and molybdenum. It's generally used in making nails, screws and early generation intramedullary nails. Cobalt Chrome implants have also been widely used in total hip arthroplasties. It is a biological inert agent but these implants are avoided in patients with nickel

allergy as it might cause metal hypersensitivity reaction (Tapscott and Wottowa, 2025).

Biocompatibility refers to how our body reacts and interacts with foreign matter. In terms of orthopedic implants, it implies how the implant will perform its function and the body has a non-pathological response to the specific implant. Majority of the implants made from stainless steel; titanium alloys and cobalt and chromium (Co-Cr) alloys have excellent biocompatibility due to their inert nature. Corrosion is also a significant factor when it comes to choosing the type of materials for implants as this process can lead to release of cytotoxic, allergenic and carcinogenic substances in the body (Al-Shalawi *et al.*, 2023).

Chromium and Cobalt are a major component of orthopedic implants and they are also a component of several enzymes in our body. Their high doses especially Cobalt can have toxic effects on our body systems leading to several symptoms of neurological, cardiological, hematological and endocrinological nature. Cobalt (Co) toxicity can cause tinnitus, vertigo, deafness and convulsions, also it can lead to hypothyroidism, polycythemia and cardiomyopathies (Sansone *et al.*, 2013). The incidence of such cases is low but literatures have put up case reports of Co-Cr toxicity after THR (Total Hip Replacement) surgeries. Cobalt toxicity in such cases can lead to anorexia, fatigue, auditory or ophthalmological damage (Samargandi *et al.*, 2024).

Metal on metal configuration in hip arthroplasty significantly elevates serum Co and Cr level as several researches have indicated and this also correlated with the increase in the level of pain (Stołtny *et al.*, 2023). There has been a case report on bilateral visual loss after multiple hip arthroplasties along with hypothyroidism and neuropathy. The patient's Co serum level was found to be >1000 µg/L (normal range 0-0.9ng/mL). There was a decrease in visual acuity in both the eyes along with bilateral temporal optic disc pallor (Garcia *et al.*, 2020). Aluminum toxicity can cause memory loss, gait disturbances and might lead to development of Amyotrophic Lateral Sclerosis. A metal-on-metal hip implant consisting of Co and Cr alloy have shown an unusual increased lymphocytic infiltration and plasma cell accumulation in the peri-prosthetic tissues as compared to other implants. In the case of hip arthroplasty with conventional implants there is no lymphocytic infiltration or plasma cells presence instead the inflammation is histiocytic predominant (Hallab *et al.*, 2001).

Chronic accumulation of Aluminum in brain can lead to development of Alzheimer's and Parkinson's disease and in kidneys can cause fibrosis in the glomeruli and Bowman's corpuscles (Peto, 2010; Ollivere *et al.*, 2012). Several studies have suggested severe complications or toxicities associated with orthopedic implants or associated metals (Table 1).

Based on the type of femoral facture different set of implants can be used to modulate the fracture such as Femoral Head, Plates, Screws, Endoprosthetic Replacements, Femoral Stems and femoral Nails. Insertion and placement of implants can lead to emotional and economic distress along with discomfort in locomotion. Patients have to go for long term treatment after surgery and physiotherapy in order to walk properly.

Global representation of femoral fracture incidence and projected trends

Due to several factors such as environmental factors, wars and conflicts injuries are most common worldwide and fractures are one of the prominent injuries that can lead to long time or short time impact on locomotion. To treat these fractures one of the treatments of choice is using orthopedic implants. One of the facts associated with implants is that they are to be implanted surgically and metallic implants remain in the body for long time ranging to years or life time. Due to ware and tare these metallic implants release toxic compounds or reactive oxygen species (ROS) that can lead to several complications in human body. A ten-year study has suggested that femoral fractures are on

rise and will be on rise as projected till 2030. Globally, hip fracture incidence demonstrates significant geographic variation, largely driven by aging populations, lifestyle changes, and healthcare access. In North America, the United States reports approximately 180–190 per 100,000 (2014), while Canadian women experience 175 per 100,000 (2021); both countries anticipate increases of 10–25% over the next two decades due to population aging (Osteoporosis Canada, 2021; Judge *et al.*, 2021). In Europe, incidence ranges from 196 per 100,000 in women and 92 in men in the UK (2018) to 205 and 97 in Germany (2019), 385 and 198 in Sweden (2010–2012), and 420 in women in Italy (2019). Trends in this region are generally stable to moderately increasing, reflecting improved survival post-fracture and advanced preventive programs (Kanis *et al.*, 2021; Piscitelli *et al.*, 2020; Xia *et al.*, 2021; Yamamoto *et al.*, 2021; Mithal and Kaur, 2018).

Table 1. Metals in femoral implants and their associated toxicities

Metal	Implant location	Associated toxicity	References
Titanium alloy	Hip stem, acetabular cup	Cytotoxicity and osteogenic differentiation	Liu *et al.*, 2025
Stainless steel	Hip stem	Cytotoxicity	Puleo and Huh, 1995
Zirconium	Femoral head and acetabular liner	Cytotoxicity and DNA damage	He *et al.*, 2020
Alumina	Femoral head and acetabular liner	Painful osteomalacia, hepatotoxicity, hypoparathyroidism, microcytic anemia	Klein, 2019
Co–Cr–Mo	Hip stem, femoral head and acetabular line	Cytotoxicity, genotoxicity, carcinogenicity and metal allergy	Zeng and Feng, 2013
Co–Cr	Hip stem, femoral head and acetabular line	Oxidative stress, carcinogenicity	Kasprzak, 2002
Ultra-high-molecular-weight polyethylene	Acetabular liner/socket	Cyto-Toxic and Oxidative stress	Gazzano *et al.*, 2011
Polytetrafluoroethylene	Acetabular liner/socket	Pathology of Liver and lungs	Schell *et al.*, 1968

In Asia, Beijing, China reports 180 per 100,000 in women and 129 in men (2008–2012), Japan 672 and 250 (2016), urban India 130 (2018), and South Korea 340 in women (2015–2018).

Rapid increases of 20–60% are projected, driven by super-aging societies, urbanization, dietary changes, and rising osteoporosis prevalence (Australian Institute of Health and Welfare [AIHW], 2023; Auckland District Health Board, 2019; Al-Elq, 2022; Rotstein *et al.*, 2022). Oceania shows similar patterns, with Australia reporting 245 and 130 (2022) and New Zealand 260 in women (2019), reflecting high life expectancy and aging populations (Rotstein *et al.*, 2022; Pinheiro *et al.*, 2020; Clark *et al.*, 2019). In the Middle East, Saudi Arabia exhibits a wide range of 51–82 (2015–2020), while Israel reports 320 in women (2016), with projected increases of 15–40% due to demographic shifts and rising osteoporosis (South African Bone Registry, n.d.). Latin America demonstrates 82 and 54 in Brazil (2015) and 87 in Mexico (2019), linked to demographic transitions and urbanization. In Africa, data remain scarce, with highly variable and under-reported incidence due to limited registries and constrained healthcare access (Oyinlola *et al.*, 2020; Robert Koch Institute and Federal Statistical Office, 2019). These findings underscore the global burden of hip fractures and highlight the need for targeted prevention and healthcare strategies adapted to regional demographics and risk factors (Table 2).

Mechanism of toxicity

One of the major toxicological effects of metals used as implants is due to their degradation (Bowsher *et al.*, 2006). Although the alloys used are inert in their nature but there is some degree of oxidation which can lead to formation of their oxides, usually present in the synovial space and metal phosphates in the extra synovial spaces. Due to subsequent wear and tear with time, corrosions lead to decrease in the size

of the particles and increase in the surface area in contact with these particles, therefore the bioactivity of these small particles is relatively increased (Liu *et al.*, 2025). Due to the small size, these particles can be easily engulfed by macrophages or can spread through lymphatic thus leading to systemic spread. Due to corrosive processes, the metal ions can also spread hematologically as they can reside in erythrocytes. Patients who have undergone management by alloy implants (Co and Cr) have shown significant increased lymphocyte reactivity to Co and Ni.

Table 2. Global representation of hip fracture incidence (as a key proxy for femoral fractures) and projected trends

Country/Region	Incidence rate (per 100,000/year)	Time period	Projected trend (Next 20 years)	Key contributing factors	Primary reference
			North America		
USA	180–190	2014	Increase 15–25%	Aging population, plateau in previous decline	Brauer *et al.*, 2009
Canada	175 (Women)	2021	Increase 10–20%	Aging population, regional variations	Osteoporosis Canada, 2021
			Europe		
United Kingdom	196 (Women), 92 (Men)	2018	Increase 10–15%	Aging population, improving post-fracture survival	Judge *et al.*, 2021
Germany	205 (Women), 97 (Men)	2019	Stable to slight increase	Good trauma care, aging demographics	RKI and DESTATIS, 2019
Sweden	385 (Women), 198 (Men)	2010–2012	Stable / Slight Decrease	Strong prevention programs, high-quality care	Kanis *et al.*, 2021
Italy	420 (Women)	2019	Increase 20–30%	One of the oldest populations globally	Piscitelli *et al.*, 2020
			Asia		
China[1] (Beijing)	180 (Women), 129 (Men)	2008–2012	Rapid increase 40–60%	Aging population, urbanization, dietary changes	Xia *et al.*, 2021
Japan	672 (Women), 250 (Men)	2016	Increase 25–35%	"Super-aging" society, high longevity	Yamamoto *et al.*, 2021
India (Urban)	130 (Women)	2018	Increase 20–30%	Rising osteoporosis, road accidents, improved diagnostics	Mithal and Kaur, 2018
South Korea	340 (Women)	2015–2018	Increase 20–25%	Rapidly aging population	Yoon *et al.*, 2021
			Oceania		
Australia	245 (Women), 130 (Men)	2022	Increase 15–20%	Aging population, high life expectancy	AIHW, 2023
New Zealand	260 (Women)	2019	Increase 10–15%	Similar demographics to Australia	Auckland DHB, 2019
			Middle East		
Saudi Arabia	51–82	2015–2020	Increase 30–40%	Rising osteoporosis, road traffic accidents, changing demographics	Al-Elq, 2022
Israel	320 (Women)	2016	Increase 15–20%	Aging population, diverse ethnic risk factors	Rotstein *et al.*, 2022
			Latin America		
Brazil	82 (Women), 54 (Men)	2015	Increase 25–35%	Demographic transition, urbanization, road accidents	Pinheiro *et al.*, 2020
Mexico	87 (Women)	2019	Increase 20–30%	Improving healthcare, rising age	Clark *et al.*, 2019
			Africa		
South Africa	Data scarce	-	Variable by region	Trauma, violence, HIV/TB comorbidity	South African Bone Registry
Nigeria	Data scarce	-	Under-reported	Road accidents, limited healthcare access	Oyinlola *et al.*, 2020

Metal ions have a well-established effect on osteoblasts thus affecting the processes of bone formation and resorption but it is still not known in depth about the effects of implant and particulate debris on the metabolism of osteoblasts.

Metal cytotoxicity can have adverse effects leading to protein damage and ultimately necrosis.

There has been research on decreased osteocalcin in the synovial fluid lining joint spaces of implants in hip arthroplasties. There has been in vitro slowing in mineralization of bone, decreased in alkaline phosphatase activity and decrease in collagen type 1 synthesis when Co and Cr were introduced. It has also been shown that these metal ions can cause a decreased in the number osteoblasts and also a change in their shapes leading to further functioning. The redox states are also affected leading to poor expression of antioxidant enzymes, and altered nitration and oxidation of proteins. This shows how implants consisting of metals like Cobalt can have significant cytotoxic effects. Osteolysis is a common manifestation which has been reported with hip arthroplasties. This is due to the overall effects of metal ions on the osteoblastic and osteoclastic activity as the disruption of balance between the process of bone formation and bone resorption leads to osteolysis, which is net bone loss. Such osteolytic lesions can present after implant introduction as cortical thinning or cyst like lesions and this raises concern for orthopedicians (Hallab *et al.*, 2001). The uptake of the metals by macrophages and osteoclasts by phagocytosis leads to the release of pro-inflammatory mediators like IL-6 and TNF-α which further activate the RANK/RANKL signaling pathway thus initiating osteolysis and inflammation (Ollivere *et al.*, 2012). Pro-inflammatory mediators like TNF-α and PGE_2 also suppress type-1 collagen generation (Vermes *et al.*, 2001).

The degradation of metal alloy implants can lead to hyper reactive response from the immune system. This reaction specifically by lymphocytes has been shown in studies where human serum from a healthy cohort was incubated at 37°C with Cobalt chromium molybdenum alloy and Titanium alloy. The lymphocyte proliferative response showed a significant increase in the serum where metal protein complexes were formed (Hallab *et al.*, 2001).

These toxic reactions elicited by femoral implants have a biochemical basis therefore several researches have been conducted to study these effects at the biochemical level. The most common pathway is through osteoclasts phagocytosis causing inflammation and osteolysis as discussed above. This leads to a vicious cycle of inflammation triggered by the re-phagocytosis of the non-degradable debris of metals (Gill *et al.*, 2012). Other chemokines like GM-CSF (Granulocyte-macrophage colony stimulating factor and M-CSF (Macrophage colony stimulate factor further stimulate inflammatory processes. The osteoclasts migrate to peri-prosthetic areas under the influence of MCP-1 (monocyte chemotactic protein-1) and MIP-1α (macrophage inflammatory protein-1α) (Magone *et al.*, 2015). The mesenchymal cell's alkaline phosphatase activity and matrix mineralization is also affected by the implant materials (Rakow *et al.*, 2016). The release of different types cytokines is depended majorly on the type of metal and its concentration. Elevation in serum concentration of Co and Cr can lead to increased levels of TNF-α (Catelas *et al.*, 2003). Increased levels of cobalt (Co) lead to increased levels of IL-1β, IL-6, IL-8, PGE_2, MCP-1, MCP-1α, INF-γ and VEGF-a (Vascular endothelial growth factor-a). Ti leads to stimulation of cytokines like IL-1β, IL-6, IL-8, PGE_2, TNF-α. also induces increased levels of MIP-1α leading to inflammation, cytotoxicity, tissue damage, DNA Damage and cancer (Zhong *et al.*, 2024) (Fig. 2).

Local tissue toxicity and clinical failure

Local tissue toxicity is a significant concern in femoral orthopedic implants, particularly in metal-on-metal (MoM) and modular components. Wear and corrosion of implant surfaces release metal ions such as cobalt (Co), chromium (Cr), and nickel (Ni) into periprosthetic tissues, which can induce cytotoxic effects on

osteoblasts, osteoclasts, and fibroblasts. This can impair bone remodeling and osseointegration, contributing to implant loosening and early clinical failure (Kurtz, 2020). Cobalt and chromium ions have been shown to generate oxidative stress, disrupt mitochondrial function, and trigger apoptosis in peri-implant cells, ultimately compromising local tissue health and implant stability (Hart *et al.*, 2021). Clinically, patients may present with pain, swelling, and soft tissue necrosis, sometimes necessitating revision arthroplasty (Clarke and Gustafson, 2000). Factors influencing tissue toxicity include implant material, modularity, surface finish, patient activity level, and individual susceptibility to metal hypersensitivity.

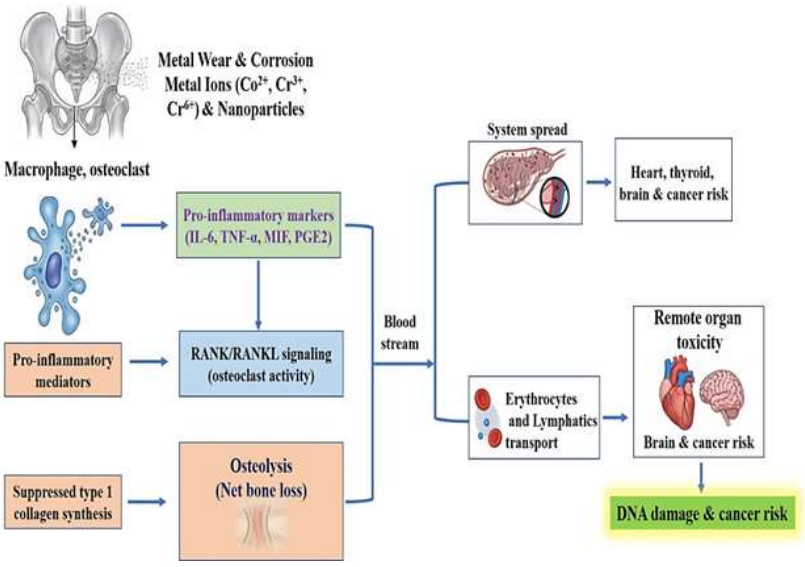

Fig. 2. Mechanism of metal on metal implant toxicity- A cellular and biochemical perspective

The foreign body response and chronic inflammation

The implantation of femoral devices initiates a foreign body response (FBR), which is a chronic inflammatory reaction characterized by macrophage activation, lymphocyte infiltration, and fibrous tissue formation. Particulate debris from polyethylene, ceramic, or metal surfaces acts as a persistent stimulus for macrophages, which release pro-inflammatory cytokines including TNF-α, IL-1β, and IL-6. These cytokines promote osteoclast differentiation and bone resorption, contributing to periprosthetic osteolysis and implant loosening (Glant *et al.*, 1996). Histologically, periprosthetic membranes surrounding implants often show macrophages, multinucleated giant cells, and lymphocytes. Chronic inflammation can compromise implant fixation and accelerate mechanical failure. Individual patient factors, including immune hypersensitivity and genetic predisposition, further modulate the severity of the response.

Key syndromes: Osteolysis, ALVAL, and pseudo tumors

Several syndromes result from local tissue toxicity and chronic inflammation around femoral implants.

Osteolysis

Is the progressive loss of bone surrounding the implant, often driven by particulate debris-induced macrophage activation. It is a primary cause of aseptic loosening and implant revision (Costa *et al.*, 2023). Early detection through imaging is critical to prevent catastrophic implant failure.

Aseptic lymphocyte-dominated vasculitis-associated lesion

ALVAL is primarily associated with MoM implants. Histopathological, ALVAL is characterized by dense perivascular lymphocytic infiltrates, tissue necrosis, and intracellular metal particles. Clinically, it presents with persistent pain, swelling, and limited mobility, frequently necessitating revision surgery

(Wu *et al.*, 2022). ALVAL severity correlates with serum metal ion levels, particularly cobalt and chromium (Hart *et al.*, 2021; Kwon *et al.*, 2022).

Pseudo tumors

Are non-neoplastic soft tissue masses that develop around implants, often asymptomatic but sometimes causing pain and mechanical impairment. They arise from chronic immune activation and tissue necrosis. Imaging, especially MRI with metal artifact reduction sequences, is critical for diagnosis. Incidence rates of pseudo tumors vary between 5–39% in MoM hip implant populations, with higher prevalence in women and patients with small-diameter femoral heads (Hasegawa *et al.*, 2024; Wakabayashi *et al.*, 2022).

Understanding the mechanisms behind local tissue toxicity, foreign body response, and these key syndromes is essential for designing safer implants, optimizing patient monitoring, and minimizing implant-related complications. Early recognition of osteolysis, ALVAL, and pseudotumor formation allows timely clinical intervention, improving long-term outcomes for patients receiving femoral orthopedic implants.

Diagnosis and risk mitigation

Early diagnosis and risk mitigation are essential to prevent clinical failure and adverse tissue reactions in femoral orthopedic implants. Patients at risk-particularly those with metal-on-metal (MoM) or modular femoral components-may present with pain, swelling, reduced range of motion, or mechanical instability. Laboratory assessment of serum cobalt and chromium levels provides early detection of excessive metal ion release, which correlates with local tissue reactions and implant wear (Hart *et al.*, 2021). Inflammatory markers such as C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) can help rule out infection but are less specific for metal-induced reactions. Combining clinical evaluation with laboratory findings allows for timely intervention before irreversible tissue damage occurs (Matharu *et al.*, 2021).

Monitoring the at-risk patient: Imaging and metal ion analysis

Vigilant postoperative monitoring is crucial for at-risk patients. Radiographs are useful for detecting gross osteolysis and implant malalignment but have limited sensitivity for early soft tissue changes. Computed tomography (CT) provides detailed evaluation of periprosthetic bone loss, while magnetic resonance imaging (MRI) with metal artifact reduction sequences (MARS-MRI) enables detection of pseudo tumors, soft tissue masses, and ALVAL-related lesions (Hasegawa *et al.*, 2024; Wakabayashi *et al.*, 2022). Ultrasound is a rapid, non-invasive adjunct for detecting fluid collections or soft tissue abnormalities.

Serial serum cobalt and chromium analysis, combined with imaging, improves risk stratification. Levels above 7 μg/L are generally considered concerning, though individual thresholds may vary based on patient factors such as renal clearance and implant type (Hart *et al.*, 2021). Early detection of elevated metal ions or periprosthetic changes allows clinicians to plan revision surgery or adjust monitoring schedules, reducing the risk of symptomatic failure.

Future directions: Advanced materials and personalized implants

Advances in implant materials and design aim to minimize adverse tissue reactions while improving longevity. High-performance alloys (e.g., titanium-molybdenum, cobalt-chromium-molybdenum) and highly cross-linked polyethylene bearings reduce wear and metal ion release (Kurtz, 2020). Surface modifications, including hydroxyapatite coatings and porous titanium structures, enhance osseointegration and reduce micromotion at modular junctions. Personalized implants, designed using preoperative imaging, computer-assisted modeling, and additive manufacturing, optimize load distribution and minimize stress shielding. Patient-specific factors, such as bone quality, activity level, and metal hypersensitivity, guide implant selection to reduce the risk of local tissue

toxicity (Matharu *et al.*, 2021). Future integration of sensor technology and "smart" implants may allow real-time monitoring of micromotion, corrosion, or osteolytic changes, enabling preemptive intervention (Robert Koch Institute and Federal Statistical Office, 2019; Wakabayashi *et al.*, 2022). Collectively, these strategies represent a shift toward precision orthopedics, enhancing clinical outcomes while mitigating toxicological complications.

Scientific novelty

Current review provides a complete insight to the toxicological implications caused due to the orthopaedic implants especially in femur. Our review is aligned with current orthopedic research and rules out any conventional literature. This review combines toxicological mechanisms with orthopedic sciences so as to understand implications from long term exposure. Article is a combination of clinical and molecular perspectives further most bridging pseudotumor formation, inflammatory pathways, aseptic lymphocyte-dominated vasculitis-associated lesions (ALVAL) and cellular responses. Additionally, review provides a distinguishing addition to the integration of global data for epidemiological, femoral and hip fractures focusing on the increasing dependence on orthopaedic implants potentially leading to toxicological burden.

Research gap

Although use of orthopedic implants in treatment of femoral factures have grown exponentially world wide but only few studies have focused on long term implications from metal ions and debris originated during corrosion, ware and tear. Also, epidemiological trends for femoral implant toxicity have not been thoroughly studied. Also, literature regarding early diagnosis and long-term monitoring is scarce that can suggest risk mitigation approaches for patients.

Future research directions

Studies should be conducted to further investigate so as to improve patient safety and implant success. Studies may focus on exploring mechanism for systemic toxicities. Development of relatively safe materials and early diagnostic procedures for possible toxicities.

CONCLUSION

Increased incidence of femur fractures has led to immense use of implants and prosthesis in the management of these fractures. This has led to a gradual increase in the concentration of metal alloys in the body and we have seen that these metal ions in a multifactorial manner can have toxicological effects on various systems of the body. The type of toxicological impact broadly depends on the type of metal alloys (physical and chemical characteristics like corrosiveness and degradability), concentration and the biocompatibility. Clinical manifestations can range from pain initially to neurological and ophthalmic manifestations like Amyotrophic Lateral Sclerosis and bilateral temporal optic disc pallor later on. Therefore, a holistic and cautious approach is extremely important for any clinician while managing patients with such conditions.

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