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Disease burden, treatment outcomes and new onset of cardiometabolic diseases and psoriatic arthritis with biologics and non-biologics in Malaysian Psoriasis Registry (MPR) patients: 10 years data

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INTRODUCTION

- Psoriasis (PsO) is an immune-mediated, chronic inflammatory disease manifesting in the skin, joints or both[1]. The estimated prevalence of PsO in Malaysia is 0.34%[2].
- The systemic inflammation in PsO is linked to a higher risk of cardiometabolic diseases (CMDs) and psoriatic arthritis (PsA)[3-6]. Systemic agents and biologic therapy are commonly used to treat moderate-to-severe PsO patients. However, there is limited understanding of the impact of these treatments on the development of CMDs and PsA in PsO patients. Understanding how biologics and non-biologics impact CMDs and PsA development in PsO patients is crucial.
- This study aims to explore the disease burden, treatment outcomes, and new onset of CMDs and PsA with biologic and non-biologic systemic treatments in adult Malaysian PsO patients.

METHODS

- This was a multicenter, cross-sectional observational study utilizing data from the Malaysian Psoriasis Registry (MPR), which, prospectively, collects data of patients with PsO treated at 36 public and 2 private hospitals in Malaysia.
- All adult PsO patients registered between January 2013 to December 2022 who had received non-biologic systemic treatment (acitretin, methotrexate, cyclosporine, or combinations) or biologics [interleukin inhibitors (IL17i, IL12/23i, IL23i) and tumor necrosis factor inhibitors (TNFi)] for at least 12 months were included in this study.
- Descriptive analyses were performed on baseline characteristics, and treatment outcomes by treatment regimens at 12 and 24 months.
- The incidence rates of new onset CMDs [ischemic heart disease (IHD), stroke, diabetes mellitus, hyperlipidemia, hypertension, non-alcoholic fatty liver disease (NAFLD)] and new onset PsA in PsO patients were compared by treatment regimens over 12 and 24 months. For this analysis, PsO patients without a diagnosis of CMDs and PsA at baseline and who had completed 12 months of treatment were included.

RESULTS

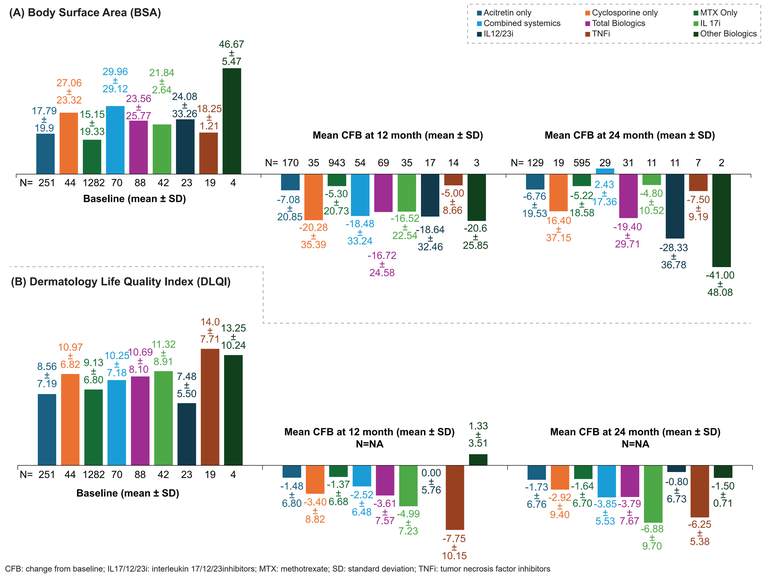
- This analysis included 1721 PsO patients. At baseline, patients on biologics were slightly younger, had earlier disease onset and diagnosis, higher psoriasis area severity index (PASI) scores, and higher family history of PsO than non-biologic patients **(Table 1)**.
- Biologic-treated patients experienced more pain, itch, and worse quality of life (QoL) than the non-biologic patients **(Table 1)**.
- At baseline, a lower proportion of patients in the biologic group reported ischemic heart disease, except those on TNFi. and none reported stroke compared to patients on non-biologics **(Table 2)**.
- Comparable proportions of patients in the biologics and MTX groups reported diabetes, hyperlipidemia, and hypertension. A greater proportion of patients in the acitretin group reported these conditions compared to all other groups (**Table 2**)
- A higher proportion of patients reported NAFLD in the biologic group compared to patients on non-biologics except for patients who received cyclosporine **(Table 2)**.
- The presence of PsA at baseline was highest in the TNFi & IL-17i groups; overall higher in the biologic group compared to non-biologic treatments **(Table 2)**.
- Patients on biologics had a higher mean body surface area (BSA) than those on non-biologics at baseline, except for those taking cyclosporine and combined systemic treatment. After 12 months, the mean BSA reduction was greater in biologic users, again with the same exception. However, at 24 months, the decrease in mean BSA was highest in biologic users compared to non-biologic treatments **(Figure 1a)**.
- Compared to the non-biologic groups, patients on biologics had higher reduction in Dermatology Life Quality Index (DLQI) scores (better QoL) at 12 months. At 24 months, the reduction in DLQI scores were comparable for biologics and non-biologics, while the IL17i biologic group had the highest reduction. **(Figure 1b)**.
- At both time points, biologic treated patients had no newly reported incidences of IHD, stroke and depression. The incidence of diabetes was lower in patients treated with biologics compared to all non-biologics except cyclosporine at 12 months and MTX, and the combined systemic group at 24 months **(Table 3)**.
- The incidence of hyperlipidemia was lower among biologic-treated patients at 12 months and cyclosporine at 24 months. Biologic-treated patients also showed a lower incidence of hypertension compared to those treated with acitretin and MTX at 12 months and cyclosporine at 24 months **(Table 3)**.
- Additionally, at 12 months, a lower PsA incidence was reported in biologic-treated patients compared to those on non-biologics, with the IL17i group remaining PsA-free. At 24 months, the non-biologic group reported a lower PsA incidence compared to those on biologics, while the IL17i and TNFi biologic groups had no new cases of PsA **(Table 4)**.

Table 1. Baseline Demographics and Characteristics of adult PsO patients in Malaysia according to treatment groups

Demographics and baseline characteristics	Acitretin only N=251	Cyclosporine only N=44	MTX only N=1282	Combined systemic treatment (>1 agent) N=70	Total Biologic N=88	IL17i N=42	IL12/23i N=23	TNFi N=19	Other Biologics (IL23i) n=4
Mean age (years) ± SD	50.1±15.4	41.5±12.1	45.9±14.9	46.3±14.3	41.2±13.1	41.4±13.3	43.6±14.0	40.1±12.6	33.5±6.1
Male - n (%)	166 (66.1)	26 (59.1)	717 (55.9)	43 (61.4)	56 (63.6)	23 (54.8)	17 (73.9)	12 (63.2)	4 (100)
Mean age of PsO onset ± SD	35.2±16.3	29.3±11.9	33.4±14.9	32.7±14.0	26.3±12.2	27.8±12.6	28.9±13.2	23.2±10.4	18.0±5.9
Mean age of PsO diagnosis ± SD	37.2±16.2	30.3±11.9	35.1±14.9	33.4±13.8	27.9±12.2	28.6±12.7	30.7±12.4	24.7±10.7	18.0±5.9
Mean weight (kg) ± SD	71.1±17.4	72.8±15.7	72.9±16.5	72.7±19.5	77.0±19.4	80.3±20.2	75.5±15.7	67.1±12.3	97.0±36.2
Mean Height (cm) ± SD	161.5±9.6	162.5±9.5	161.6±9.1	161.9±10.4	163.9±9.8	163.0±10.8	164.6±8.7	163.1±8.8	173.4±6.1
Mean BMI (kg/m2) ± SD	27.2±6.1	27.5±5.3	27.9±6.0	27.7±7.0	28.7±7.2	30.3±7.7	27.9±5.9	25.5±6.0	31.8±10.2
Family history of PsO - n (%)	61 (24.3)	10 (22.7)	326 (25.4)	17 (24.2)	31 (35.2)	15 (35.7)	9 (39.1)	6 (31.6)	1 (25)
Duration of psoriasis (years, mean) ± SD	15.8±10.6	12.4±9.3	12.5±9.2	14.2±8.6	14.8±9.0	13.9±10.7	14.8±8.0	16.9±6.7	15.5±2.9
Mean PASI ± SD	7.4±8.2	9.3±8.3	8.0±10.1	14.2±14.8	20.1±15.5	21.7±17.0	18.9±15.4	14.1±9.4	25.6±11.4
Itch - n (%)	51 (20.3%)	12 (27.3%)	272 (21.2%)	21 (30%)	27 (30.7%)	21 (50%)	5 (21.7%)	0 (0%)	1 (25%)
Pain - n (%)	7 (2.8%)	4 (9.1%)	58 (4.5%)	4 (5.7%)	7 (8%)	5 (11.9%)	2 (8.7%)	0 (0%)	0 (0%)
Mean baseline DLQI ± SD	8.6±7.2	11.0±6.8	9.1±6.8	10.2±7.2	10.7±8.1	11.3±8.9	7.5±5.5	14.0±7.7	13.2±10.2
Ethnicity - n (%)									
Malay	115 (45.8)	21 (47.7)	631 (49.2)	32 (45.7)	44 (50)	21 (50)	10 (43.5)	10 (52.6)	3 (75)
Chinese	91 (36.3)	12 (27.3)	303 (23.6)	23 (32.9)	28 (31.8)	11 (26.2)	10 (43.5)	6 (31.6)	1 (25)
Indian	26 (10.4)	7 (15.9)	186 (14.5)	12 (17.1)	11 (12.5)	7 (16.7)	3 (13)	1 (5.3)	0 (0)
Others	19 (7.6)	4 (9.1)	162 (12.6)	3 (4.3)	5 (5.7)	3 (7.1)	0 (0)	2 (10.5)	0 (0)

Total Biologics= IL17i + IL12/23i + TNFi + Other Biologics (IL23i)\
DLQI: dermatology life quality index; IL17/12/23i: interleukin 17/12/23 inhibitors; MTX: methotrexate; PASI: psoriasis area severity index; SD: standard deviation; TNFi: tumor necrosis factor inhibitors

Figure 1. Treatment Outcomes: BSA and DLQI at baseline, 12 and 24 months



CFB: change from baseline; IL17/12/23i: interleukin 17/12/23inhibitors; MTX: methotrexate; SD: standard deviation; TNFi: tumor necrosis factor inhibitors

Table 2. Baseline Comorbidities of adult PsO patients in Malaysia according to treatment groups

Comorbidities	Acitretin only N=251	Cyclosporine only N=44	MTX only N=1282	Combined systemic treatment (>1 agent) N=70	Total Biologic N=88	IL17i N=42	IL12/23i N=23	TNFi N=19	Other Biologics (IL23i) n=4
Ischaemic heart disease - n (%)	12 (4.8%)	1 (2.3%)	53 (4.1%)	1 (1.4%)	1 (1.1%)	0 (0%)	0 (0%)	1 (5.3%)	0 (0%)
Stroke - n (%)	4 (1.6%)	0 (0%)	16 (1.2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Diabetes mellitus - n (%)	61 (24.3%)	5 (11.4%)	239 (18.6%)	16 (22.9%)	16 (18.2%)	8 (19%)	2 (8.7%)	6 (31.6%)	0 (0%)
Hypertension yes - n (%)	96 (38.2%)	14 (31.8%)	373 (29.1%)	26 (37.1%)	29 (33%)	15 (35.7%)	6 (26.1%)	7 (36.8%)	1 (25%)
Hyperlipidemia - n (%)	94 (37.5%)	9 (20.5%)	312 (24.3%)	21 (30%)	22 (25%)	9 (21.4%)	5 (21.7%)	7 (36.8%)	1 (25%)
Depression - n (%)	0 (0%)	0 (0%)	4 (0.3%)	0 (0%)	1 (1.1%)	1 (2.4%)	0 (0%)	0 (0%)	0 (0%)
Fatty liver (NAFLD) - n (%)	2 (0.8%)	4 (9.1%)	26 (2.0%)	1 (1.4%)	8 (9.1%)	6 (14.3%)	2 (8.7%)	0 (0%)	0 (0%)
PsA - n (%)	36 (14.3 %)	8 (18.2%)	422 (32.9%)	28 (40%)	39 (44.3%)	24 (57.1%)	1 (4.3%)	13 (68.4%)	1 (25%)

IL17/12/23i: interleukin 17/12/23inhibitors; MTX: methotrexate; NAFLD: non-alcoholic fatty liver disease; PsA: psoriatic arthritis; TNFi: tumor necrosis factor inhibitors; SD: standard deviation

Table 3. Treatment Outcomes: New Incidence of CMDs at 12 and 24 months

Cardiometabolic Diseases (CMDs)		Acitretin only	Cyclosporine only	MTX only	Combined systemic treatment (>1 agent)	Total Biologic	IL17i	IL12/23i	TNFi	Other Biologics (IL23i)
Incidence of comorbidities post 12- and 24-months treatment *(n/N), %*										
Ischemic heart disease	12 mo.	1/237 (0.4%)	1/42 (2.4%)	13/1206 (1.1%)	0/69 (0%)	0/80 (0%)	0/39 (0%)	0/22 (0%)	0/15 (0%)	0/4 (0%)
	24 mo.	1/160 (0.6%)	0/29 (0%)	6/788 (0.8%)	0/39 (0%)	0/33 (0%)	0/14 (0%)	0/10 (0%)	0/7 (0%)	0/2 (0%)
Stroke	12 mo.	2/244 (0.8%)	0/43 (0%)	5/1243 (0.4%)	0/70 (0%)	0/80 (0%)	0/39 (0%)	0/22 (0%)	0/15 (0%)	0/4 (0%)
	24 mo.	1/160 (0.6%)	0/31 (0%)	0/805 (0%)	0/40 (0%)	0/32 (0%)	0/13 (0%)	0/10 (0%)	0/7 (0%)	0/2 (0%)
Diabetes mellitus	12 mo.	6/190 (3.2%)	0/38 (0%)	39/1027 (3.8%)	3/54 (5.6%)	1/64 (1.6%)	0/31 (0%)	1/19 (5.3%)	0/10 (0%)	0/4 (0%)
	24 mo.	5/117 (4.3%)	2/26 (7.7%)	19/654 (2.9%)	0/28 (0%)	1/27 (3.7%)	0/12 (0%)	0/8 (0%)	0/5 (0%)	1/2 (5%)
Hypertension	12 mo.	17/155 (10.9%)	1/29 (3.5%)	67/893 (7.5%)	2/44 (4.5%)	3/53 (5.6%)	1/25 (4.0%)	0/16 (0%)	2/9 (22.2%)	0/3 (0%)
	24 mo.	3/93 (3.2%)	4/19 (21.1%)	16/546 (2.9%)	0/22 (0%)	2/21 (9.5%)	0/8 (0%)	1/8 (12.5%)	0/4 (0%)	1/1 (100%)
Hyperlipidemia	12 mo.	15/157 (9.6%)	2/34 (5.8%)	92/950 (9.7%)	4/49 (8.1%)	3/60 (5.0%)	1/31 (3.2%)	1/17 (5.8%)	1/9 (11.1%)	0/3 (0%)
	24 mo.	5/91 (5.5%)	4/22 (18.2%)	34/578 (5.9%)	1/27 (3.7%)	2/23 (8.7%)	1/9 (11.1%)	0/8 (0%)	0/5 (0%)	1/1 (100%)
Depression	12 mo.	0/132 (0%)	1/26 (3.8%)	1/633 (0.2%)	0/35 (0%)	0/58 (0%)	0/33 (0%)	0/15 (0%)	0/6 (0%)	0/4 (0%)
	24 mo.	1/76 (1.3%)	0/16 (0%)	1/354 (0.3%)	0/14 (0%)	0/17 (0%)	0/7 (0%)	0/6 (0%)	0/2 (0%)	0/2 (0%)
Fatty liver (NAFLD)	12 mo.	7/125 (5.6%)	1/21 (4.7%)	11/604 (1.8%)	0/33 (0%)	2/52 (3.8%)	0/29 (0%)	0/13 (0%)	2/6 (33.3%)	0/4 (0%)
	24 mo.	4/67 (6%)	1/15 (6.7%)	12/342 (3.5%)	1/12 (8.3%)	0/18 (0%)	0/8 (0%)	0/6 (0%)	0/2 (0%)	0/2 (0%)

CMDs: Cardiometabolic diseases; IL17/12/23i: interleukin 17/12/23inhibitors; mo: months; MTX: methotrexate; NAFLD: non-alcoholic fatty liver disease; TNFi: tumor necrosis factor inhibitors

Table 4. Treatment Outcomes: New Incidence of PsA at 12 and 24 months

Psoriatic Arthritis (PsA)	Acitretin only	Cyclosporine only	MTX only	Combined systemic treatment (>1 agent)	Total Biologic	IL17i	IL12/23i	TNFi	Other Biologics (IL23i)
Post 12 Months Treatment									
New onset (incidence) *(n/N), %*	11/215 (5.12%)	5/36 (13.89%)	68/866 (7.85%)	5/43 (11.63%)	2/51 (3.92%)	0/20 (0%)	1/21 (4.76%)	1/7 (14.29%)	0/3 (0%)
PsA incidence rates per 1000 patient-years (95% CI)	51.16 (25.54–91.54)	138.9 (45–324)	78.52 (60.98–99.5)	116.28 (37.80–271.40)	39.21 (4.75–141.60)	0 (0–0)	47.62 (121–265.32)	142.8 (3.6–795.9)	0 (0–0)
PsA Incidence – Odds ratio (95% CI) [Total biologics vs each non-biologic]	1	1	1	1	Vs. Acitretin:0.757 (0.162–3.525) Cyclosporine:0.253 (0.046–1.385) MTX:0.479 (0.114–2.012) Combined Syst: 0.310 (0.057–1.687)	-	-	-	-
Post 24 Months Treatment									
New onset (incidence) *(n/N), %*	8/139 (5.76%)	0/24 (0%)	32/563 (5.68%)	2/22 (9.09%)	2/27 (7.41%)	0/10 (0%)	1/10 (10%)	0/5 (0%)	1/2 (50%)
PsA incidence rates per 1000 patient-years (95% CI)	57.55 (24.85–113.4)	0 (0–0)	56.84 (38.88–80.24)	90.91 (11.01–328.39)	74.07 (8.97–267.5)	0 (0–0)	100 (2.5–557)	0 (0–0)	500 (12.7–2785)
PsA Incidence – Odds ratio (95% CI) [Total biologics vs each non-biologic]	1	1	1	1	Vs. Acitretin:1.310 (0.262–6.537) Cyclosporine:4.803 (0.219–105.221) MTX:1.327 (0.301–5.854) Combined Syst: 0.800 (0.103–6.191)	-	-	-	-

CI: confidence interval; I IL17/12/23i: interleukin 17/12/23inhibitors; MTX: methotrexate; PsA: psoriatic arthritis; TNFi: tumor necrosis factor inhibitors; Vs: versus

CONCLUSIONS

- PsO patients treated with biologics had better improvement in disease severity and QoL, as well as a reduced risk of developing CMDs and PsA compared to those on non-biologic treatments. Notably, only the patients treated with IL-17i remained free from PsA over two years.
- Early biologic treatment initiation may help improve treatment outcome and reduce the risk of new onset of CMDs and PsA in PsO patients.

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